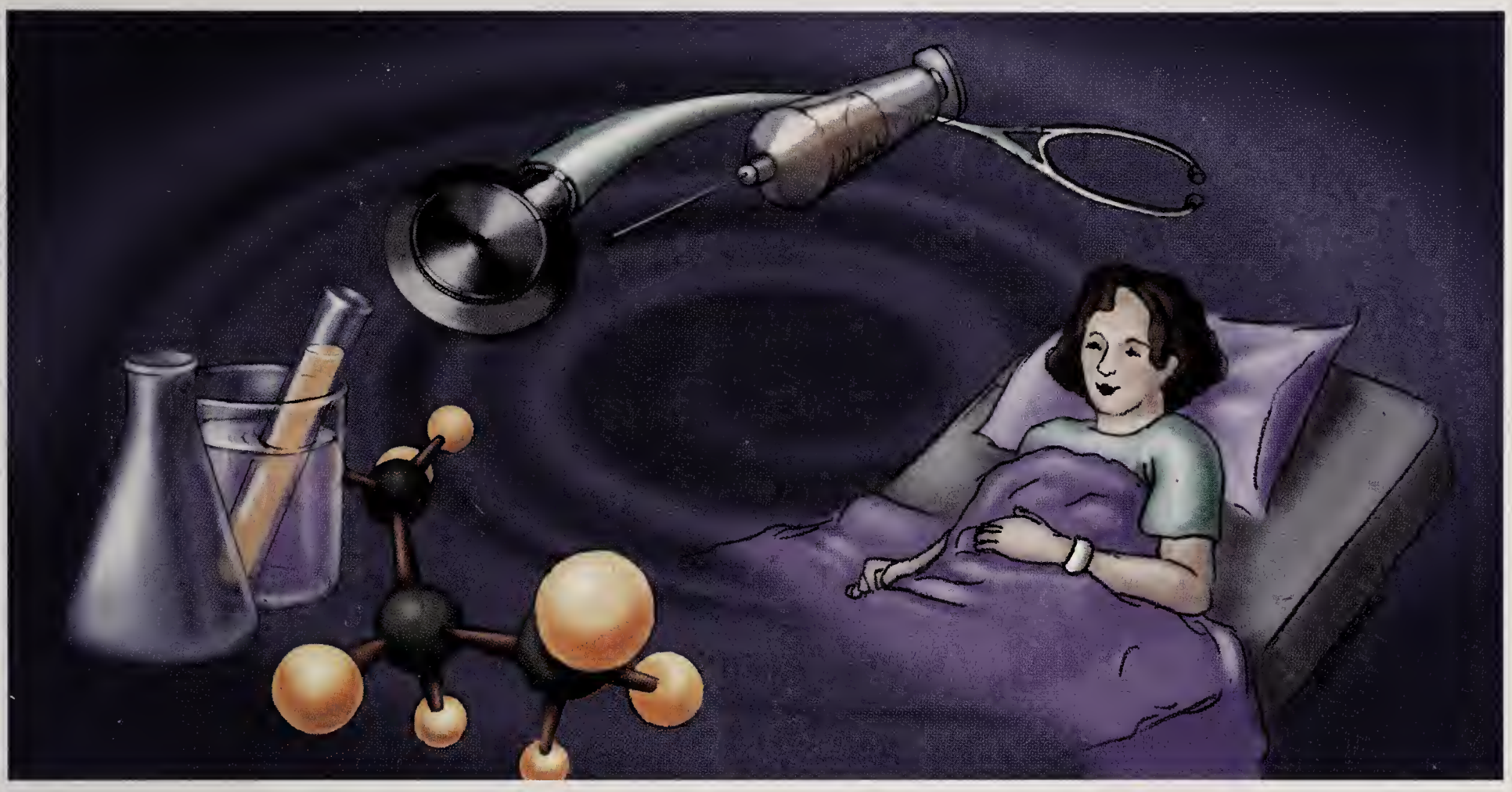
UTMJ

University of Toronto Medical Journal

VOLUME 76, NUMBER 3 / MAY 1999



***UTMJ* FOCUS SERIES: Evidence-Based Medicine**

140 **Glossary**
Evette Weil

142 **Evidence-Based Medicine: Part 1**
Defining Evidence-Based Medicine
Sean Wharton

144 **Evidence-Based Medicine: Part 2**
From Clinical Trials to the Clinic
Evette Weil

148 **Evidence-Based Medicine: Part 3**
Usefulness of Evidence-Based Medicine to Medical Students and a Guide to the Use of Evidence-Based Medicine
Mark Benaroia

150 **Evidence-Based Medicine: Part 4**
Making Sense of the Numbers
The United Kingdom Prospective Diabetes Study (UKPDS-38) – Treating Hypertensive Diabetic Patients
Sean Wharton

152 **Bed Use on a Maltese Medical Ward: Implications for the Treatment of the Complications of Diabetes**
Ann Bugeja, and Joseph Azzopardi

158 **An Introduction to Transcranial Magnetic Stimulation and Its Use in the Investigation and Treatment of Depression**
Dan Mozeg, and Edred Flak

164 NEWS AND VIEWS

179 MORNING REPORT

183 CLINICOPATHOLOGICAL CORRELATION

189 QUICK DIAGNOSIS

194 TECHNOLOGY REVIEWS

200 BOOK REVIEWS

Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalMay1999uoft

UTMJ
University of Toronto Medical Journal
Founded In 1923 Volume 76, No. 3 May 1999

TABLE OF CONTENTS

UTMJ Focus Series

Evidence-Based Medicine
140 Glossary
Evette Weil

142 Evidence-Based Medicine: Part 1
Defining Evidence-Based Medicine
Sean Wharton

144 Evidence-Based Medicine: Part 2
From Clinical Trials to the Clinic
Evette Weil

148 Evidence-Based Medicine: Part 3
Usefulness of Evidence-Based Medicine to Medical Students and a Guide to the Use of Evidence-Based Medicine
Mark Benaroia

150 Evidence-Based Medicine: Part 4
Making Sense of the Numbers
The United Kingdom Prospective Diabetes Study (UKPDS - 38) - Treating Hypertensive Diabetic Patients
Sean Wharton

Public Health

152 Bed Use on a Maltese Medical Ward: Implications for the Treatment of the Complications of Diabetes
Ann Bugeja, and Joseph Azzopardi

Neuropsychiatry

158 An Introduction to Transcranial Magnetic Stimulation and Its Use in the Investigation and Treatment of Depression
Dan Mozeg, and Edred Flak

News and Views

164 In the Literature: The *UTMJ* Club

166 *UTMJ* Series on Complementary and Alternative Medicine (CAM) Part 3:
Homeopathy: Has it Beaten Medicine at its Own Game?
Dan Perri

170 The Cuerrier Decision: Public Health and the Criminalization of HIV Serostatus Non-Disclosure
Darrell Tan

174 Keeping Doctors North: Recruiting and Retaining Physicians in Underserviced Areas
Jason A. Shack, and Alison D. Baker

Morning Report

179 The Dwindles
Ra Han, Mark Benaroia, and Barry J. Goldlist

Clinicopathological Correlation

183 Case of Confusion
Joanna Holland

Quick Diagnosis

189 Emergency Medicine Rounds
Thomas Roger Harris, and Laura Catherine McAdam

Technology Reviews

194 Robots Designed to Aid in Surgical Procedures
Martin Jugenburg

Book Reviews

196 Stroke: Pathophysiology, Diagnosis, Management, Third Edition

198 Clinical Neuroimmunology

200 The Massachusetts General Hospital Guide to Psychiatry in Primary Care

Front cover illustration by Karen Petruccelli
Division of Biomedical Communications,
Department of Surgery, University of Toronto.

Editorial

Here is the third and final installment of Vol. 76 of the *UTMJ*. With this issue we close yet another chapter in the long and illustrious history of the Journal. We believe that this issue will provide, like so many before, an enjoyable and thought provoking look at medical science. Lets take a quick look at the pages of our final issue.

In this issue we present two excellent original articles from very different areas of medicine. Mozeg *et al.* present a highly informative review on transcranial magnetic stimulation for the diagnosis and treatment of depression. While Bugeja *et al.* have written a fascinating review on diabetes and ressource allocation. Moreover, in this focus issue on evidence based medicine, we have compiled a series of short articles and a glossary of frequently used terms that will introduce students to the sometimes complex but always important aspects of evidence based practice. We believe that this section will prove to be a highly valuable learning tool that will continue in the years to come.

In addition, the News and Views section keeps our readers abreast of current events with two reviews of highly newsworthy stories. Tan has authored a report on the recent criminalization of HIV spread by the supreme court. Baker and Shack have reviewed the important issue of physician underservicing in the North of Canada. Moreover, Morning Report presents the clinical reasoning behind a case of infective endocarditis whereas this issue's discussion in Clinicopathological Correlation relates to an interesting case of dementia. We also continue our series on complementary and alternative medicine which has been a highlight of this year.

With this issue we mark the end of our tenure as editors of the Journal. We have enjoyed this unique experience and are honored to have had the opportunity to be a part of a great tradition of the Faculty of Medicine at the University of Toronto. However, we could not have done this alone. We extend our deepest gratitude to our associate editors who orchestrated the entire peer review process and to the many students and staff who patiently reviewed each submission. Moreover, we thank the many section editors that have worked incredibly hard throughout the year to provide us with thought provoking and interesting articles. We are also indebted to the multi-talented illustrators whose contributions grace each cover and improve the aesthetics of each article. We must also thank the many contributors whose works appeared in the pages of the Journal. Laslty, we are also very grateful for the continued support that we have received from our patrons and the Medical Society.

Finally, we look to the future editors and their staff to continue the long legacy of the *UTMJ* and uphold the high standards of this Journal. We are confident that they will prove to be successful.

Sincerely,

Sandra Demaries, MSc.
George Thanassoulis, BSc.
Editors-in-Chief

UTMJ

Editors-In-Chief:
Sandra L. Demaries, MSc. (MD/PhD2)
George Thanassoulis, BSc. (0T1)

Associate Editors
Richard Bitar, MSc. (0T1)
Julian Mathoo, MSc. (0T1)

Managing Editor
Phyllis Billia, Ph.D (0T1)

Treasurer
Elaine Yeung, BA (0T1)

Art Director
Kevin Millar

News & Views Editors
Andrew Lustig, BSc. (0T0)
Sean Wharton, PharmD (0T1)

Quick Diagnosis Editors
Thomas Harris, BSc. (0T1)
Laura McAdam, MSc. (0T1)

CPC Editors
Jonathan Grynspan, BSc. (0T0)
Joanna Holland, MSc. (0T1)

Morning Report Editor
Mark Benaroia, BSc. (0T1)
Ra Han, Bsc. (0T0)

Technology Review Editors
Martin Jugenburg, BSc. (0T1)

Book Review Editor
Paul Giacomini, BSc. (0T1)

Website Directors
Michael Szeto, BSc. (0T1)

Copy Editors
Raymond Fung, BSc. (0T1)
Adrian Harvey, MSc. (0T1)

Secretary
Joan Caverly

Editorial Board
Victoria Atkinson, BSc. (0T1)
Dr. Andrew Baines, MD, FRCPC
Gillian Edmonds, MSc. (0T1)
David Kaplan, MSc. (0T1)
Michelle Lambert, MSc, (0T1)
Dr. Robert Levitan, MD, FRCPC
Eric Saettler, Ph.D (0T1)
Dr. Mladen Vranic, MD, DSc., FRCPC, FRSC

Biomedical Communications
Zacharo Roula Drossis
Monique Le Blanc
Kevin Millar
Karen Petruccelli
Chesley Sheppard

Design Consultant
Nancy Nowacek, MA

Typesetting
Type & Graphics

Patrons

The UTMJ Staff wishes to thank the following patrons for their generous donations:

BENEFACTOR OF THE UTMJ

Dr. Sharon M. Abel
Dr. K.S. Amankwah
Dr. Aubie Angel
Dr. Joanne Bargman
Dr. Daniel C. Cattran
Dr. Paul Dedumets
Dr. John Edmonds
Dr. Ronald S. Fenton
Dr. D.M. Goldberg
Dr. David S. Goldbloom
Dr. Larry Grossman
Dr. Patrick Gullane
Dr. Ian J. Harrington
Dr. Robert Haslam
Dr. E. Jenny L. Heathcote
Dr. Bob Hilliard
Dr. Irwin Hilliard
Dr. William J. Horsey
Dr. Michael J. R. Howcroft
Dr. Michael Hutcheon
Dr. Robert Hyland
Dr. Gabor P. Kandel
Dr. Terence Kavanaugh
Dr.& Mrs. A.J. Kennedy
Dr. Jay Keystone
Dr. Douglas Kondziolka
Dr. Stephen Kraft
Dr. Richard Lamon
Dr. Allan W. Luxton
Dr. O.J. Mandel
Dr. J. T. Marotta
Dr. Robert Maunder
Dr. Rosemary Meier
Dr. Bruce S. Mutter
Dr. Charles Peniston
Dr. James R. Perry
Dr. Mel Petersiel
Dr. Eliot A. Phillipson
Dr. Anita Rachlis
Dr. Kenneth J. Reed
Dr. Robin Richards
Dr. Donato A. Ruggiero
Dr. M. Lynn Russell
Dr. John Rutka
Dr. Irving E. Salit
Dr. Robert B. Salter
Dr. Micheal Sarin
Dr. Hugh E. Scully
Dr. George Y. Takahashi
Dr. Graham Trope
Dr. William S. Tucker
Dr. Catharine Whiteside
Dr. Wendy L. Wolfman
Dr. Douglas E. Yates

PATRON OF THE UTMJ

Dr. Arnold Aberman
Dr. Mary Jane Ashley
Dr. Andrew Baines
Dr. Michael A. Baker
Dr. Eric J. Barker
Dr. David Byers
Dr. Howard M. Clarke
Dr. J.J. Connon
Dr. Paul Cotterill
Dr. Christopher R. Forrest
Dr. Gordon Froggatt
Dr. Kan Ying Fung
Drs. Joan S. & Richard M. Gladstone
Dr. Barry J. Goldlist
Dr. Michael L. Guinness
Dr. Richard J. Inman
Dr. Andrew G. James
Dr. Bruce W. Knox
Dr. Robert Kyle
Dr. F. Lista
Dr. Ray D. Martin
Dr. Andrew W. Maykut
Dr. Hugh D. McGowan
Miller Bernstein & Partners
Dr. Heather S. Morris
Dr. Bruce S. Mutter
Dr. Richard I. Ogilvie
Dr. Gregory Olscamp
Dr. John D. Parker
Dr. K.P.H. Pritzker
Dr. Joseph E. Rogers
Dr. Janet M. Roscoe
Dr. Irving E. Rosen
Dr. Bernie Silverman
Dr. Leslie E. Soper
Dr. Albert C. Strickler
Dr. D.J.A. Sutherland
Dr. John R. Taylor
Dr. Ronald W. Taylor
Mr. P. Thanassoulis
Dr. Hugh G. Thompson
Dr. Martin G. Unger
Dr. Walter P. Unger
Dr. James Waddell
Dr. Gary Webb
Dr. Peter M. Webster
Dr. David Wesson
Dr. E. D. Wigle

FRIEND OF THE UTMJ

Dr. Douglas J. Alton
Dr. Crawford S. Anglin
Dr. Sylvia L. Asa
Dr. Susan Belo
Dr. Earl Bogoch
Bracken Library - Queen's
Dr. T. Douglas Bradley
Dr. Brian Butler
Canada Institute for STI
Dr. A. Cecutti
Dr. Albert Cheskes
Dr. Robert Chisholm
Dr. Bernard Cinader
Dr. Edward H. Cole
Dr. John G. Connolly
Dr. Donald H. Cowan
Dr. Helen P. Demshar
Dr. H. Roslyn Devlin
Dr. Terence A. Doran
Dr. Sheila K. Doyle
Dr. Stuart Z. Dyment
Dr. Gerald Edelist
Dr. Armis Freiberg
Dr. Steven Gallinger
Dr. Arthur Geisler
Dr. Donald A. Gibson
Dr. Alan L. Goldbloom
Dr. Jamie D. Graham
Dr. Wendy C. Graham
Dr. Ian Graham
Dr. Leonard F. Grover
Dr. Mary E. Hannah
Dr. Sophie L. Hofstader
Hospital For Sick Children
Dr. R. J. Howard
Dr. Masanori Ichise
Dr. Michael Jewett
Dr. Margaret Jury
Dr. Armand Keating
Dr. John D. Kempston
Ms. Christine Kreutzer
Dr. C.D. Lambert
Dr. Bernard Langer
Dr. Brian Leong-Poi
Dr. Sam L. Librach
Dr. William K. Lindsay
Dr. Alick Little
Dr. Konstantin R. Loewig
Dr. D. I. Lorenzen
Dr. Paul Marks
Dr. Jaanus Marley
Dr. Steven McCabe
Dr. Nancy H. McKee
Dr. Martin McKneally
Dr. Robin McLeod
Dr. David McNechy
Dr. David Mendelssohn
Dr. Ernest R. Michel
Ms. Donna Mikola
Dr. David Mock
Dr. Robert Moore
Dr. Paul J. Muller
Dr. Martin G. Myers
Dr. Salim Z. Naqvi
Dr. A. John B. Nazareth
Dr. Allan Okey
Dr. Diana Omylanowski
Dr. Howard Ovens
Dr. Fred R. Papsin
Dr. H. Pasternak
Dr. Robert L. Patten
Dr. Walter J. Peters
Dr. Anne Phillips
Dr. G. L. Ralph
Dr. Donald A. Redelmeier
Dr. W. John Reynolds
Dr. Robert N. Richards
Dr. Frank W. Rosenberg
Dr. Robert L. Ruderman
Dr. Fred Saibil
Dr. Jerry Shime
Dr. Barry Shrott
Dr. Ken H. Shumak
Dr. Mel Silverman
Dr. Ivan Silver
Dr. Katherine Siminovitch
Dr. Allan R. Slomovic
Dr. Carlton G. Smith
Dr. John C. Stears
Taichung Veterans
Dr. Ian Tannock
Dr. Lorne M. Tarshis
Dr. Charles T. Tator
The Yao Trust
Dr. Marvin Tile
Dr. Mary Trotter
Dr. Murray B. Urowitz
Dr. Robert Wald
Dr. S. Joseph Weinstock
Dr. Richard D. Weisel
Woodward Library - Serials
Dr. Cecil Yip
Dr. Ron Zuker

The editors apologize for any omissions to the above list; this list represents our final version at press time. We will update the list in future issues.

Evidence-Based Medicine Glossary

Evette Weil, BA (0T2)

Welcome to the UTMJ's Focus Series on evidence-based medicine. This series of short articles is intended to serve as an introduction to a critical area of modern medical practice. The editors wish to thank Sean Wharton (0T1) for editing the series, and Dr. Andrew Baines for critical review of the articles.

Evidence-based medicine utilizes a language of clinical epidemiological terms. To understand and critically appraise research articles, the physician must have a grasp of these concepts. The following glossary is provided as an introduction and reference tool to be used in applying EBM principles to the literature. The terms are adapted from a glossary published online by the Evidence-Based Medicine Working Group at the University of Alberta. (http://www.med.ualberta.ca/ebm/ebm.htm)

Karen Petruccelli

Absolute risk

The observed or calculated probability of an event in the population under study.

Absolute risk reduction (ARR)

The difference in the absolute risk (rates of adverse events) between study and control populations.

Blinded study (Syn: masked study)

A study in which observer(s) and/or subjects are kept ignorant of the group to which the subjects are assigned, as in an experimental study, or of the population from which the subjects come, as in a non-experimental or observational study. Where both observer and subjects are kept ignorant, the study is termed a double-blind study. If the statistical analysis is also done in ignorance of the group to which subjects belong, the study is sometimes described as triple blind. The purpose of "blinding" is to eliminate sources of bias.

Case-series

Report of a number of cases of disease.

Case-control study
Retrospective eomparison of exposures of persons with disease (eases) with those of persons without the disease.

Cohort study
Follow-up of exposed and non-exposed defined groups, with a eomparison of disease rates during the time eovered.

Confidence interval (CI)
The range of numerieal values in whieh we ean be eonfident (to a eomputed probability, sueh as 90 or 95%) that the population value being estimated will be found. Confidenee intervals indieate the strength of evidence; where eonfidence intervals are wide, they indicate less preeise estimates of effeet.

Incidence
The number of new cases of illness eommeneing, or of persons falling ill, during a speeified time period in a given population.

Intention to treat analysis
A method for data analysis in a randomized elinieal trial in whieh individual outeomes are analyzed aeeording to the group to whieh they have been randomized, even if they never reeeived the treatment they were assigned. By simulating practieal experienee it provides a better measure of effectiveness.

Likelihood ratio
Ratio of the probability that a given diagnostie test result will be expeeted for a patient with the target disorder rather than for a patient without the disorder.

Number Needed to Treat (NNT)
The number of patients who must be exposed to an intervention before the elinieal outeome of interest oeeurred; for example, the number of patients needed to treat to prevent one adverse outeome.

Odds
A proportion in whieh the numerator eontains the number of times an event occurs and the denominator ineludes the number of times the event does not oeeur.

Odds Ratio (Syn: cross-product ratio, relative odds)
A measure of the degree of assoeiation; for example, the odds of exposure among the eases eompared with the odds of exposure among the controls.

Predictive value
In screening and diagnostie tests, the probability that a person with a positive test is a true positive (i.e., does have the disease), or that a person with a negative test truly does not have the disease. The predietive value of a sereening test is determined by the sensitivity and speeificity of the test, and by the prevalenee of the eondition for whieh the test is used.

Prevalence
The proportion of persons with a partieular disease within a given population at a given time.

Prospective study
Study design where one or more groups (eohorts) of individuals who have not yet had the outeome event in question are monitored for the number of sueh events that oeeur over time.

Randomized controlled trial
Study design where treatments, interventions, or enrollment into different study groups are assigned by random alloeation rather than by eonseious deeisions of clinicians or patients. If the sample size is large enough, this study design avoids problems of bias and eonfounding variables by assuring that both known and unknown determinants of outeome are evenly distributed between treatment and eontrol groups.

Relative risk (RR)
The ratio of the probability of developing, in a speeified period of time, an outeome among those reeeiving the treatment of interest or exposed to a risk faetor, compared with the probability of developing the outeome if the risk faetor or intervention is not present.

Relative risk reduction (RRR)
The extent to whieh a treatment reduees a risk, in eomparison with patients not reeeiving the treatment of interest.

Retrospective study
Study design in which cases where individuals who had an outeome event in question are eolleeted and analyzed after the outeomes have oeeurred.

Sensitivity (of a diagnostic test)
The proportion of truly diseased persons, as measured by the gold standard, who are identified as diseased by the test under study.

Specificity (of a diagnostic test)
The proportion of truly nondiseased persons, as measured by the gold standard, who are so identified by the diagnostie test under study.

Validity
The extent to whieh a variable or intervention measures what it is supposed to measure or aeeomplishes what it is supposed to aeeomplish. The internal validity of a study refers to the integrity of the experimental design. The external validity of a study refers to the appropriateness by whieh its results ean be applied to non-study patients or populations.

for such interest and the principles underlying the practice of EBM. The UTMJ article in this issue, by Evette Weil, addresses the principles underlying the practice of EBM.

Reasons for the Interest in EBM

The main reason for the increased interest in EBM is that it address three major problems in clinical practice; the inability to manage large volumes of medical information, the difficulty in containing rising medical costs, and the desire to optimize patient care with current, up to date therapeutic options.

a) Information Management

Physicians are interested in learning how to practice EBM in an attempt to manage the vast amount of medical information that is now available. The need for new, clinically relevant data is essential for a practice that strives to achieve the optimal medical management of patients. Physicians are sensitive to this issue, yet are incapable of processing the volumes of information necessary to keep up to date. Self reports from enthusiastic clinical teachers place their medical reading time at only 2 hours per week, yet general physicians must read 19 original articles a day 365 days a year, if they want to remain informed within their own field.[3] This expectation is obviously unattainable. Therefore physicians are constantly in search of rapid solutions to bring their knowledge up to the level of recent advances. Continuing medical education (CME) attempts to address this concern, yet research has demonstrated that CME is often ineffective at modifying clinical behaviors and at improving health outcomes of patients.[4]

EBM attempts to provide clinicians with the tools to develop their own methods of continuing education, especially in situations that can be immediately applied to the patient. Altering clinical practice and improving patient care are practical steps that are inherent in the EBM process. EBM provides a method of condensing the volumes of information available into an applicable approach that reflects the best evidence. Development of a structured question from the clinical case, a focused search of the literature, critical appraisal and the use of systematic reviews, overviews and guidelines are all methods employed in EBM to address the difficulty in accessing medical information.[5]

b) Medical Cost Constraints

The economic climate of the 1990s has required politicians, patients, and physicians to assess the cost of medical care. The focus of maximizing the limited resources to provide the best care is a national issue that continues to be of concern to the majority of Canadians. EBM attempts to provide clinicians with a broad perspective on health economics, emphasizing best practices that improve the health of patients in the most cost-effective manner. This method of practice preserves scarce resources for future medical concerns. The application of practice guidelines, pharmacoeconomic analysis, and cost-effectiveness studies is promoted by EBM.[6] Clinician practicing EBM are sensitive to the economic environment and can make macro-decisions based on information from large populations rather than individual cases.

c) Optimizing Patient Care

Most importantly, practicing patient-specific EBM will provide each patient with the optimal level of care. Decisions made regarding a patient's medical management will be based on a combination of best available evidence, clinical judgement and expertise, cost effective therapies, and patient preference.[1] Clinicians may argue that this approach has always been a part of patient management, yet EBM formalizes this process and provides the clinician with information that has been comprehensively reviewed by the leaders in the field.

The practice of evidence based medicine is probably not a fad. Specific terminology may change over time but the concepts introduced with EBM will become more common within medical practice as medical students begin to learn the benefits of this approach. Medical students and residents will follow the lead of opinion leaders, many that have pioneered the field of EBM, and will learn the benefits and pitfalls of this approach.[1,2,5,7,8] Hopefully, the methods of EBM will assist in resolving the three problems areas within clinical practice, resulting in improved ability to access and integrate new information, realize cost containment and optimize patient care using the best evidence available.

References

1. Haynes RB, Sackett DL, Gray JMA, Cook DJ, Guyatt GH. (1996). Transferring evidence from research into practice: 1. The role of clinical care research evidence in clinical decisions. *Evidence-Based Medicine.* 1(7):196-197.
2. Sackett DL Rosenborg WMC, Gray JA, Haynes RB, Richardson WS. *BMJ.* (1996). 312:71-2.
3. Davidoff F, Haynes B, Sackett D, Smith R. (1995). Evidence based medicine. A new journal to help doctors identify the information they need. *BMJ* 310:1085-6.
4. Sibley JC, Sackett DL, Neufeld VR, *et al.* (1982). A randomized trial of continuing medical education. *N Engl J Med* 306:511-5.
5. Oxman AD, Sackett DL, Guyatt GH. (1993). Users Guides to the medical literature. 1. How to get started. *JAMA* 270(17):2093-2095.
6. Laupacis A, Fenny D, Detsky AS, Tugwell PX. Tentative guidelines for using clinical and economic evaluations revisited. *CMAJ.* 1993;18(6):927-929.
7. Detsky AS. (1995). Regional variations in medical care. *N Engl J Med.* 333(9):589-590.
8. Guyatt GH, Rennie D. (1993). Users guide to the medical literature. *JAMA* 270(17):2096-2097.

Evidence-Based Medicine Series: Part 1

Defining Evidence-Based Medicine

Sean Wharton, BScPhm, PharmD (0T1)

An Introduction to the Evidence-Based Medicine Series

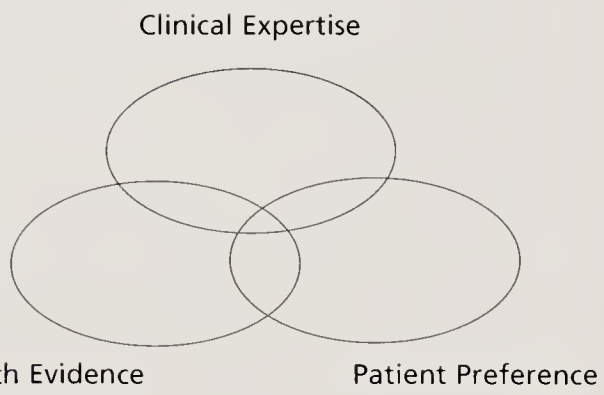
Evidence based medicine (EBM) has rapidly become a popular method of clinical practice among health care professionals. The *UTMJ* series on EBM will introduce readers to the various aspects of this new paradigm. The first three articles in this series are presented in this issue and will discuss the concepts behind the establishment of EBM, the practical aspects of using this approach and the usefulness of EBM for medical students. Future issues of the *UTMJ* will feature articles from opinion leaders within the field of EBM. These articles will address the controversies associated with the implementation and acceptance of EBM. As this series develops we hope that readers will gain insight into EBM and will consider the importance of practicing EBM in their medical careers.

EBM is an approach to medical practice that has been initiated by a broad coalition of clinicians, researchers, educators, and policy makers to accelerate and improve the application of evidence from sound clinical care research to clinical practice.[1] The editors of the Evidence Based Medicine Journal have used the following definition of EBM.

Definition

Evidence based medicine is the conscientious and judicious use of current best evidence from clinical care research in the management of individual patients.[2]

EBM patient management incorporates three distinct components; clinical expertise, patient preference, and research evidence. (see Figure 1) This model addresses the point that clinical expertise and patient preference can override research evidence. Examples include a clinical decision not to operate on a patient who is too frail, although the evidence indicates that surgery is the best option, or a patient preference not to take the medication that clinical circumstances and research indicate is best for her condition.[1]



Adapted from Haynes et al. EBMJ 1996

Figure 1. *A model for evidence-based clinical decisions.*

The interest in EBM has dramatically increased in the past five years. Noting the increase in EBM articles listed on MEDLINE easily validates this point. A focused search on MEDLINE using the key words "evidence based medicine" produces no citations between the years of 1985 to 1990, eight citations from 1991 to 1995, and a shocking 876 citations from 1996 to 1999. Such a dramatically increased interest in a new approach to medical practice should inspire any astute clinician to investigate both the reasons

Evidence-Based Medicine Series: Part 2

From Clinical Trials to the Clinic

Evette Weil, BA (0T2)

The Rise of Evidence-Based Medicine

Evidence-based medicine (EBM) is a philosophy of medical practice that emphasizes the value of scientific evidence as a basis for determining patient care. Evidence has long been an integral part of medicine, but this new discipline formally advocates "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients."[1] This approach does not contend that scientific evidence is the only valid input into clinical decisions, but rather that the best available data should be incorporated with clinical experience and common-sense to provide the highest standard of care. Traditionally, physicians have based much of their clinical decision-making on professional training, textbooks, personal experience and expert opinions. The evidence-based medicine model seeks to preserve this conventional base of knowledge while supplementing it with quantitative information from methodologically sound studies.

A number of factors have contributed to the emergence of evidence-based medicine as a new paradigm of clinical practice. These include the extraordinary volume of published literature, variations in physicians' practices, and increased economic pressure to contain health care spending. It has been estimated that the average family physician would have to read 19 articles per day everyday of the year to remain current on best medical practice.[2] Even if the appropriate 19 articles are selected, this magnitude of reading is an unrealistic expectation for the majority of physicians. Therefore, the first goal, of evidence-based medicine is to make the most relevant and influential information easily available to physicians. This has largely been accomplished via electronic databases, such as Medline and Cancerlit, which have become both more user-friendly and widely accessible through the internet. As database-searching capabilities have improved, physicians are increasingly able to find exactly the information they need without sifting through excessive amounts of extraneous information.

The second goal of EBM is to decrease the variability between physicians in areas where certain practices are clearly associated with superior outcomes. This variance has been well documented in a number of cases, including the prescription of beta-blockers following myocardial infarction, as well as the performance of common surgical procedures such as peripheral revascularization and mastectomy.[3,4] Much of this incongruity can be explained by the absence of evidence in clinical decision-making, with the accessibility and utilization of clinical research lying at the crux of the question of practice variability. Both a change in physician attitude toward the value of clinical research in everyday practice and an increased availability of relevant information are needed to reduce such discrepancies.

The final goal of EBM is to minimize health care costs while maximizing health care benefits. We live in an era of intensifying economic constraints on health care. As newer, more expensive tests and therapies are introduced into practice, there is an increasing need to determine the value of any innovation. Concurrently, there is an increasing demand for quality and sensitivity to individual patient preferences. These sometimes opposing forces have made it necessary to clearly and quantitatively understand the improvements offered by a novel diagnostic test or treatment. Thus, evidence-based medicine goes hand in hand with cost-benefit studies which try to incorporate efficacy, quality of life, and monetary costs.

Practicing Evidence-Based Medicine

How does the busy physician practice evidence-based medicine? As detailed below, there are four essential steps: formulating the question, searching for data, critical appraisal, and applying the information to individual patients.

1. Formulating the Question

Many questions arise in the course of treating a patient related to the optimal diagnostic tests, therapies, and prognosis. Evidence-based medicine requires that these decision points be expressed as focused clinical questions. For example, the physician may ask: What is the sensitivity of this diagnostic test? Or what is the risk of recurrence following a specific chemotherapeutic regimen? The key here is that the question is constructed such that it can be answered with demonstrable, quantitative data. The benefit of a focused clinical question is that it limits the required search.

2. Searching the Literature

2.1 Guidelines

There are multiple sources of information, which require varying degrees of analysis from the searching physician. (Figure 1) At the top of the hierarchy are guidelines published by various professional societies, non-profit organizations and government agencies. These guidelines are particularly valuable, because they represent the combined analysis of multiple experts in the field who have exhaustively examined and appraised the breadth of relevant research. Guidelines generally examine multiple facets of an issue, such as efficacy, cost, and patients preferences. Therefore, their conclusions usually become the standard of care.

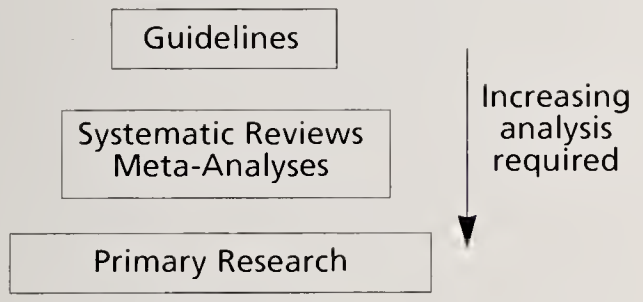


Figure 1. *Hierarchy of evidence.*

2.2 Systematic Reviews and Meta-analyses

Systematic reviews and meta-analyses lie at the next level. These studies survey all of the evidence in a particular area, and attempt to summarize the findings in qualitative and quantitative terms. The benefit of these two methods is that they help amalgamate large volumes of information, thereby increasing accessibility to published research. The challenge for the physician is that not all systematic reviews and meta-analyses are conducted equally well. In appraising such analyses, the physician should explore whether the researchers have clearly outlined a complete search strategy and how they have accounted for heterogeneity between input studies.

2.3 Primary Literature

Finally, there will be questions that are not adequately addressed by either published guidelines or systematic reviews/meta-analyses. In this case, the physician will need to investigate the original research to find an answer. As mentioned above, the increased availability and improved searching capabilities of electronic databases have greatly facilitated this process. As might be expected, these searches require more work. The physician will most likely have to examine multiple trials, and evaluate the validity of all of the findings. However, some reports have suggested that an effective search and article retrieval need only take 30 minutes to complete provided the question is limited and well-defined.[5]

3. Critical Appraisal

Once the search is complete (this is particularly relevant for original research trials) the evidence has to be critically appraised. A number of worksheets have been assembled to aid physicians with this task—an example of which is depicted in Figure 2.[6] Questions that should be asked include: Was the appropriate study design chosen? How significant are the findings? Was the trial blinded and randomized? Were the appropriate patients selected? To simplify this process, a newer abstract format has been adopted by some journals which includes some of the information necessary for critical appraisal. If the results of the trial appear sound and convincing, the physician can then transpose the findings from the trial to the clinical setting.

1 Are the results of the study valid?
a) Was the assignment of patients to treatments randomized?
b) Were all patients who entered the trial properly accounted for and attributed at its conclusion?
- Was follow-up complete?
- Were patients analyzed in the groups to which they were randomized

c) Were the patients, health workers and study personnel "blind" to treatment?
d) Were the groups similar at the start of the trial?
e) Aside from the experimental intervention, were the groups treated equally?

2. What were the results?
a) How large was the treatment effect?
b) How precise was the estimate of the treatment effect?

3. Will the results help me in caring for my patients?
a) Can the results be applied to my patient care?
b) Were all clinically important outcomes considered?
c) Are the likely treatment benefits worth the potential harms and costs?

Source: Adapted from Guyatt GH, et al.

Figure 2. *Guide to Critical Appraisal.*

4. Application to Individual Patients

The final step is to apply the evidence to the individual patient. This requires that the physician determine both the applicability of the finding to the patient and integrate the evidence with clinical experience and expertise. In order to obtain internal validity, most clinical trials exclude many of the patients who are seen in everyday medicine such as the elderly or patients with multiple co-morbidities. To make the necessary clinical decisions, it is the responsibility of the clinician to understand the complexity of a single case. This involves using clinical reasoning, intuition, and the assembled evidence.

Evidence-Based Medicine Resources

As the emerging paradigm of evidence-based medicine has increased in dominance in recent years, a host of evidence-based medicine resources have become available. These include centers devoted to the discipline, collections of guidelines and systematic reviews, journals with the aim of presenting digests of clinical trials, workshops, and continuing medical education (CME), undergraduate, and postgraduate courses in evidence based medicine. The following is a description on some of the principal resources:

Centres

1. Institute for Clinical Evaluative Sciences (ICES). A non-profit research organization dedicated to conducting research that contributes to the effectiveness, quality and efficiency of health care in Ontario. The website provides extensive information on best practices, caremaps, and current research information. An interesting feature is the Practice Atlas Series which details variations in physician practices and health care delivery across the province. Homepage: http://www.ices.on.ca
2. Health Information Research Unit (HIRU) at McMaster University. A pioneer in the field of evidence-based medicine. The department conducts research in the field of health information science and is dedicated to the development of new information systems to support EBM. HIRU is also the base for the Canadian Cochrane Centre, is a partner in the Evidence-Based Practice Center program, and hosts the editorial office for five EBM journals. Homepage: http://www.hiru.mcmaster.ca
3. Center for Evidence Based Medicine (CEBM). An academic centre, based in Oxford, England devoted to advancing EBM research and aiding EBM practitioners. The centre supports Critical Appraisal for Medical Students (CAMS), an international student group which provides opportunities for students to develop the basic skills needed to practice EBM. Homepage: http://cebm.jr2.ox.ac.uk/
4. Agency for Health Care Policy Research (AHCPR). A U.S. government agency which supports many evidence-based medicine projects. They develop guidelines, and have published 19 sets to date. They also sponsor a program of 12 Evidence-Based Practice Centers in the U.S. and Canada that will produce reports and technology assessments on important clinical topics. Homepage: http://www.ahcpr.gov.
5. Center for Evaluation of Medicines (CEM). A multidisciplinary research organization affiliated with St. Joseph's Hospital and McMaster University, which examines a range of issues important to the optimization of therapeutic interventions. The goal of CEM is to improve physician prescribing behaviour. Homepage: http://www.thecem.net/overview.htm

Print Resources

- *User's Guide to the Medical Literature Series* in the *Journal of the American Medical Association (JAMA)*. A series of EBM guides for physicians written by researchers at McMaster University with contributions from colleagues across North America. The Series starts in the November 3, 1993 edition (vol 270, no. 17) and continues for the following year. Topics include searching the literature, critical appraisal, and applying results to real patients.
- *American College of Physicians (ACP) Journal Club.* The journal summarizes and comments on articles from the biomedical literature that warrant immediate attention by physicians attempting to keep pace with important advances in internal medicine. Homepage: http://hiru.mcmaster.ca/acpjc/p&plong.htm
- *Evidence Based Medicine.* A bimonthly publication from the *British Medical Journal (BMJ)* and the American College of Physicians (ACP). The journal surveys 70 international journal for key research relevant to clinical practice. Homepage: http://www.bmjpg.com/data/ebm.htm
- *Evidence-Based Nursing.* New journal designed to address important EBM issues in nursing. Contains summaries of significant research and commentary with each article from expert sources. Homepage: http://www.bmjpg.com/data/ebn.htm
- *Evidence-Based Mental Health.* Publication designed to link mental health research to psychiatric practice. Homepage: http://www.psychiatry.ox.ac.uk/cebmh/journal/
- *Journal of Evidence-Based Health Care.* Provides managers and health policy makers with the best evidence available about the financing, organization and delivery of health care. Homepage: http://www.ihs.ox.ac.uk/ebhc/
- *Best Evidence.* A CD-ROM published yearly containing collected articles from the ACP Journal Club and Evidence-Based Medicine. Homepage: http://hiru.mcmaster.ca/acpjc/acpod.htm
- *Clinical Evidence.* A compendium produced by BMJ and ACP of the best available research findings on common and important clinical questions (updated and expanded every six months). The first issue will be available in book format in June 1999. Homepage: http://www.bmjpg.com/data/ebm.htm

Electronic Resources

1. Electronic databases, such as Medline and Cancerlit, are available through multiple internet portals, including the University of Toronto library and the National Library of Medicine. Homepages: http://ot.library.utoronto.ca/ovidweb/ovidweb.cgi, , http://www.medportal.com
2. Cochrane Collaboration. A nonprofit, international organization that prepares, organizes, and maintains systematic reviews of health care interventions. The main product is the Cochrane Library, which is updated quarterly and distributed by disk, CD-ROM or via the internet. The library includes databases of internally prepared systemic reviews, abstracts and critical assessments of other reviews, a register of controlled trials, and information on critical appraisal methodology. Homepage: http://www.cochrane.co.uk.
3. National Guideline Clearinghouse. A partnership between the AHCPR, the American Medical Association, and the American Association of Health Care Plans with the goal of making detailed information on clinical practice guidelines widely available to health professionals. Homepage: www.guideline.gov.
4. ICES and CEBM websites. These websites provide a comprehensive assortment of EBM resources. They are linked to many of the journals and EBM centers. Particularly noteworthy are the tools available on both sites to be used in critical appraisal of the literature. The aids include guides for searching the literature, comparison of study designs, quality filters to assess studies, and specific statistical devices for calculating likelihood rations and other measures. See the centres' homepages.

References

1. Sackett DL, Rosenberg WMC, Muir Gray JA. (1996). Evidence-Based Medicine: What it is and What it isn't. *BMJ* 312:71-2.
2. Straus SE, Sackett DL. (1998). Getting Research Findings into Practice: Using Research Findings in Clinical Practice. *BMJ* 317:339-42.
3. O'Connor GT, Quinton HB, Traven ND, *et al.* (1999). Geographic Variation in the Treatment of Acute Myocardial Infarction:The Cooperative Cardiovascular Project. *JAMA* 281:627-33.
4. Birkmeyer JD, Sharp SM, Finlayson SR, Fisher ES, Wennberg JE. (1998). Variation Profiles of Common Surgical Procedures. *Surgery* 142-917-23.
5. Evidence-Based Medicine: A New Approach to Teaching the Practice of Medicine. Http://hiru.mcmaster.ca/ebm/overview.htm.
6. Guyatt GH, Sackett DL, Cook DJ, *et al.* (1994). Users' Guides to the Medical Literature: II. How to Use an Article About Therapy or Prevention. *JAMA* 271: 59-63.

BUILD YOUR FUTURE WITH US

The Health Services Restructuring Commission has directed that Ross Memorial Hospital will play a strengthened role in the delivery of health care in Victoria County and the surrounding area, promoting the expansion and enhancement of services. Positions are available immediately in Family Medicine and in some specialty areas. The hospital has 147 beds to be increased to 218 by 2003. A state-of-the-art birthing unit was recently completed. Ross Memorial Hospital in Lindsay, Ontario serves a population of approx. 70,000 and lies in the heart of the Kawarthas, offering an outstanding lifestyle and a wide range of urban amenities.

ROSS MEMORIAL HOSPITAL

For more information, contact:
Dr. S.M. Young, Chief of Staff at (705) 324-6111,
Dr. P. Anderson, Chief of Family Medicine, (705) 324-2037,
Dr. P. Ursel, Chief of Emergency Medicine, (705) 324-6111.

Visit us on the web at www.rmh.org

PETERS-BOYD ACADEMY

MEDICUS SERVIT, SERVAT DEUS

at Sunnybrook
& Women's College
Health Sciences Centre

In Support of Our Medical Society

We have more compound interest than most banks.

Over the last 40 years, no one
has developed more pharmaceutical
compounds than we have.
Absolutely no one.

Janssen-Ortho Inc.
19 Green Belt Drive, North York, Ontario, Canada M3C 1L9

WESTERN HEALTH CARE CORPORATION

CORPORATE OFFICE
PO BOX 2005
CORNER BROOK, NF
A2H 6J7

We serve a large geographic region with a population of approximately 95,000 in Western Newfoundland, Canada. Currently we are recruiting family practitioners and specialists eligible for registration with the *Newfoundland Medical Board* to work in communities, hospitals and medical clinics of the region. Our priority needs are residency trained physicians as follows:

Physicians
Family Practitioners
Psychiatrists
Anaesthetists
Obstetricians and Gynaecologists

All interested applicants should call
Medical Affairs
at 709-637-5548 or 709-643-5111 (x 416)
or submit CV's to
fax number 709-637-5410

Evidence-Based Medicine Series: Part 3

Usefulness of Evidence-Based Medicine to Medical Students and a Guide to the Use of Evidence-Based Medicine

Mark Benaroia, BSc. (OT1)

Undergraduate medicine is a time when most students begin to develop a primitive construct in regards to the approach of learning new information.[1a] Methods of how to store, use, and evaluate information are also established. Medical school is also a time when mentors, teachers, and experts have the most influence on the development of this systematic approach to solving medical problems. It becomes apparent that effective and efficient ways of dealing with new information, should be taught during medical school. Unfortunately many medical students are not exposed to evidence based medicine. This leads to the following question, are medical students being taught the most effective methods of problem solving?

Many medical students, are taught to adopt the dogma of current practice, and to learn from the experts in the field.[1] Although we are in the midst of a paradigm shift in regards to the use of EBM, most teaching of evidence-based practice occurs at the level of the resident. Indeed, one could argue that learning the skill of critical appraisal would have had more utility if taught in medical school, therefore increasing the number of years of practicing this logical approach to medicine. This point is emphasized in a paper summarizing the various studies assessing effectiveness of teaching critical appraisal skills to medical students and residents.[2] Norman and Shannon found that four out of six studies reviewed involving medical students showed consistent evidence that critical appraisal courses of varying lengths, using a variety of teaching methods, greatly increased basic knowledge of topics in clinical epidemiology; this knowledge was determined by a written test.[2-8] Overall, the mean difference in test scores between those receiving instruction and controls was 17% (SD 4%). One of the studies concluded that continued use of critical appraisal skills by medical student's are required for maintaining those large gains.[3] On the contrary, four studies reviewed involving teaching EBM to residents showed small gains in knowledge in tests subjects.[9-12] Overall, the mean difference in test scores between those receiving instruction and controls was 1.3% (SD 1.7%) over the control subjects. This review demonstrates that early instruction in EBM is necessary to actualize the practice of EBM.

1a A primitive construct is a personalized method for learning and understanding new information

Understanding and Implementing the Practice of EBM

How should medical students attempt to implement evidence-based thinking in their studies? The following steps will guide students in understanding the practice EBM. The first and most important step that medical students should take is to accept that all aspects of medicine are imperfect. Learning about clinical diagnosis and treatments is often accomplished by unsystematic observation from senior physicians who may not emphasize the use of evidence. Learning through anecdotal experience without evidence is an incomplete practice of medicine. Therefore the second step towards understanding EBM is to review the principles established by the Evidence-Based Medicine Working Group.[1] Briefly, there are three principles established by this group:

1) Clinical experience and clinical instincts are paramount to becoming a practitioner and are particularly important in situations where procedures of diagnosis, for example, are not tested. Pathophysiologic principles

are essential in defining the questions and seeking the evidence. Furthermore, in the absence of evidence, which is often the case, all that is left to work with is pathophysiological principles. However, when evidence is available and clinical decisions have been made in its absence, one must remain skeptical and critical.

2) The study of the basic mechanisms of disease are necessary but insufficient guides for clinical practice. The principle message is for one not to rely on pathophysiological principles alone, and to always seek the evidence.
3) The interpretation of literature on causation, prognosis, diagnostic tests, and treatment, requires an understanding of rules of evidence as practiced in EBM.

These principles imply that practitioners and medical students regularly consult the literature and be able to critically appraise these papers. Additionally, it is important that medical students accept that evidence does not exist for many aspects of medicine and that even with appropriate literature, students may lack understanding due to their level of training.

After reviewing the basic principles governing the use of EBM, it is suggested by one author[13] that medical students use a proactive approach to practicing EBM. This approach consists of taking an active role in understanding EBM and how it can be incorporated into practice. Evidently, the amount of literature can be intimidating so it is suggested that a resource that is short and simple is found. Most importantly, students should never lose site of the ultimate goal – treating patients more effectively.

The next step is to learn how to ask answerable questions about patients, search for and critically appraise articles, and summarize data in a succinct one-page draft. This can be learned by consulting web sites on available courses (McMaster University http://hiru.mcmaster.ca/ebm/) or by consulting the literature such as the JAMA series on Evidence Based Medicine.[1] This process could be overwhelming so it is important not to feel obligated to learn this process under a time constraint. Start generating questions about topics that you are interested in that may be specific to treatment or diagnosis about patient's that you encounter (e.g. are ACE inhibitors the most optimal treatment for hypertension?). Once a question is generated search for articles in a database that you are comfortable with such as MEDLINE. Alternatively, use databases, such as the Cochrane Library, that contain articles which are considered to be the best evidence in a field. Read the appropriate articles and create a summarized one-page report of your findings. As you become more familiar with the process and your skills become more refined, set a goal for yourself such as completing one summarized report per week. Once a library of these summarized reports are created they could be used as quick reference guides for you or your colleagues. Medical students in their clinical years should try to apply this evidence to the patients they treat, but first consult the resident or attending. Medical students in their pre-clinical years could apply their knowledge in group settings such a problem-based learning sessions, clinical courses, or seminars.

Medical students are currently taught to adopt the dogma of current practice and learn from experts in the field. While learning traditionally through expert opinion is an important part of the medical curriculum, critically appraising what we are taught or the information being taught will assist us in becoming innovators rather than followers. Ask yourself the following: Are we being taught in the most effective way possible? Are we being taught to think critically about diagnosis and treatment? This is precisely where evidence-based medicine comes in. By taking a proactive approach to learning EBM you could positively influence the development of your clinical knowledge and thus how you will practice medicine in the future.

References

1. Evidence-Based Medicine Working Group. Evidence-Based Medicine: A new approach to teaching the practice of medicine. (1992). *J. AMA* 268:2420-25.
2. Norman GR, Shannon SI. (1998). Effectiveness of instruction in critical appraisal (evidence-based medicine) skills: A critical appraisal. *Can Med Assoc J* 158:177-81.
3. Riegelman RK. (1986). Effects of teaching first-year medical students skills to read medical literature. *J Med Educ* 61:454-60.
4. Bennett KJ, Sackett DL, Haynes RB, Neufld VR, Tugwell P, Roberts RS. (1987). A controlled trial of teaching critical appraisal of the clinical literature to medical students. *JAMA* 257:2451-54.
5. Frasca MA, Dorsch JL, Aldag JC, Christiansen RG. (1992). A multidisciplinary approach to information management and critical appraisal instruction: a controlled study. *Bull Med Libr Assoc* 80:23-7.
6. Landry FJ, Pangaro L, Kroenke K, Lucey C, Herbers J. (1994). A controlled trial of a seminar to improve medical student attitudes toward, knowledge about, and use of the medical literature. *J Gen Intern Med* 9:436-9.
7. Heller RF, Peach H. (1984). Evaluation of a new course to teach the principles and clinical applications of epidemiology to medical students. *Int J Epidemiol* 13:533-7.
8. Radack KL, Valanis B. (1986). Teaching critical appraisal and application of medical literature to clinical problem solving. *J Med Educ* 61:329-31.
9. Gehlbach Sh, Bobula JA, Dickinson JC. (1980). Teaching residents to read the literature. *J Med Educ* 55:362-5.
10. Linzer ML, Brown JT, Frazier LM, DeLong ER, Siegel WC. (1988). Impact of a medical journal club on house staff reading habits, knowledge and critical appraisal: a randomized controlled trial. *JAMA* 260:2537-41.
11. Linzer M, DeLong ER, Hupart KH. (1987). A comparison of two formats for teaching critical reading skills in a medical journal club. *J Med Educ* 62:690-2.
12. Kitchens J, Pfeiffer MP. (1989). Teaching residents to read the medical literature: a controlled trial of a curriculum in critical appraisal/clinical epidemiology. *J Gen Intern Med* 4:385-7.
13. Ball C. (1999). Evidence-based medicine on the wards: report from an evidence-based minion. *ACP Journal Club* 130:A15-A16.

Evidence-Based Medicine Series: Part 4

Making Sense of the Numbers

The United Kingdom Prospective Diabetes Study (UKPDS - 38) – Treating Hypertensive Diabetic Patients

Sean Wharton, BScPhm, PharmD (0T1)

Using the statistical tools of critical appraisal is crucial when reviewing the results of an article. It is necessary for clinicians to apply in house statistics, as any particular treatment can result in differing degrees of benefit depending on the patient situation. This is not an easy task, as many clinicians and students will accept the results presented in the study and will not attempt to further analyze the results. There are many article that address statistical critical appraisal. An article by David Sackett in *Evidence-Based Medicine,* and the *Users Guide to the Medical Literature II,*[1, 2] reviewed some basic, essential statistical measures.

Evidence based medicine (EBM) can help a clinician determine whether treatment A is better than treatment B for a specific patient. The United Kingdom Prospective Diabetes Study (UKPDS-38) trial is described in the 'In the Literature' section of this journal. This trial randomized hypertensive patients with Type 2 diabetes to "tight" versus "less tight" blood pressure control (BPC). The patients with tight BPC had fewer diabetes related complications and fewer deaths due to diabetes compared to the patients with less tight BPC. Over 8 years of treatment 16.3% of patients died in the less tight BPC group, compared to 11% in the tight BPC group. What do these numbers tell us in regards to treating patients? To apply these statistics to patients we need to calculate the absolute risk reduction, the relative risk reduction, and the number needed to treat. This can be accomplished simply be designing a 2 by 2 table. For this table the clinician will need the actual numbers of patients in the study.

	OUTCOME (Deaths)		
	-ve outcome (death)	+ve outcome (alive)	Totals
Treatment A (tight control)	a) 84	b) 674	758
Treatment B (less tight control)	c) 64	d) 326	390

Relative Risks

RRa - The relative risk of Treatment A causing the neg. outcome (death) is a/a+b = 11%

RRb - The relative risk of Treatment B causing the neg. outcome (death) is c/c+d = 16.3%

RR - The relative risk of death occurring in treatment A compared to treatment B is RRa/RRb = (a/a+b)/(c/c+d) = 0.674

Relative risk reduction (RRR)

RRR - The relative risk reduction is a figure frequently quoted and is calculated by subtracting the RR from 1; (1-RR) x 100% = (1-0.674) x 100% = 32.5%

Absolute risk reduction (ARR)

ARR - The absolute risk reduction is simply the difference between the outcome rates in the two treatment groups; RRb-RRa = 0.63-0.11 = 0.053 = 5.3%.

RRR compared to the ARR

The relative risk reduction (RRR) is useful as it indcates that 1 in 3 of the expected deaths were prevented by tight BPC.

But the RRR fails to discriminate absolute treatment effects from those that are trivial. Therefore the use of the ARR gives us a concrete number to determine the size of the effect. The ARR of 5.3% indicates that with tight control, you will save 5.3% of patients from death. One describes the reduction in events (32.5% fewer deaths) and the other describes the reduction in persons affected (5.3% fewer patients died). One advantage of the ARR is that it exemplifies the relationship between the therapeutic effort (treating 100 people) and the clinical yield (saving 5.3 lives).[3]

Number Needed to Treat (NNT)

NNT = 1/ARR

An alternate way of expressing this relationship between therapeutic effort and clinical yield is by taking the inverse of the ARR or 1/5.3% = 19. This is referred to as the NNT. In the current case, you need to treat 19 patients for 8 years to prevent 1 death from diabetes.

This example illustrates that RRR usually is a big number (eg.32.5%), and as such they appeal to researchers trying to demonstrate impressive results. The ARR may appear a lot less impressive (5.3%). The NNT (19) highlights the effort necessary to achieve the desired outcome. Other questions can be generated from these numbers. For example is it cost effective to treat 19 patients to save one life? Is 19 patients a good NNT? The answer to these questions has to do with clinical significance not statistical significance. This NNT of 19 is fairly small and the cost of antihypertensive therapy is relatively affordable. In comparison, if you had the same RRR of 32.5%, with a ARR of 0.53% it would result in a NNT of 188. Once cost and side effects are taken into consideration this NNT is obviously less favourable.[3] Yet, without completing these calculations, a clinician would have considered that a RRR of 32.5% was quite impressive and may consider using Treatment A, for his patients.

With these considerations in mind, physicians can determine whether one treatment is better that another, and if so, if there is a significant enough improvement in outcome to favour one treatment over another.

Future issues of the *UTMJ* will contain examples of how to use odds ratios, effect sizes, confidence intervals and other statistical parameters.

References

1. Dryver E. (1998). The numbers you need to treat your patients. *Informed* 5(1):8.
2. Guyatt GH. Sackett DL. Cook DJ. (1994). Users guide to the medical literature. II. How to use an article about therapy or prevention. B. What were the results and will they help me in caring for my patients? *J. IMA* 271(1):59-63.
3. Sackett DL. O (1996). some clinical useful measures of the effect of treatment. *Evidence-based Medicine* 1(2):37-38.

Physician Opportunities for:

Family Practice Physician	Gastroenterologist	Anaesthesiologist
Emergency Room Physician	Medical Oncologist	Adult Psychiatrist
Dermatologist	Radiation Oncologist	Child Psychiatrist
Rheumatologist	Radiologist	Forensic Psychiatrist

Health Care Leader

The Cape Breton Healthcare Complex is a progressive health care leader. It operates a regional hospital, three community hospitals, a comprehensive cancer centre, a rehabilitation centres and several long term care centres. The complex has 450 acute care beds and over 200 physicians.

Scenery, culture, more....

The sea, mountains, and lakes make Cape Breton a great place to live, work and play.

For information contact:

Dr. M. A. Naqvi, Medical Director
Cape Breton Healthcare Complex
1482 George Street
Sydney, Nova Scotia B1P 1P3

Fax: (902) 567-7921
E-Mail: mnaqvi@cbhc.ns.ca

General/Family Practice Opportunities in Brant County

This southwestern Ontario community offers full hospital services to support solo and group practice family medicine. Prime access to academic centres, located midway between Toronto and London and 20 minutes from Hamilton on Hwy. 403. Community amenities include parks, shopping, golfing, educational institutions, an airport and spousal employment opportunities.

Incentive grants available from the Ministry of Health to attract 17 general/family physicians to urban and rural practices in Brantford, Paris and Brant County. See us at http://bfree.on.ca/recruit or call for details on practices inviting new partners or available existing practices.

To discuss opportunities, contact:
Brant Physician Recruitment Group
c/o Grand River District Health Council
233 Colbourne St., Ste. 304
Brantford, Ontario
N3T 2H4
Tel (519) 756-1330 Fax (519) 756-6013
info@grdhc.on ca

Bed Use on a Maltese Medical Ward: Implications for the Treatment of the Complications of Diabetes

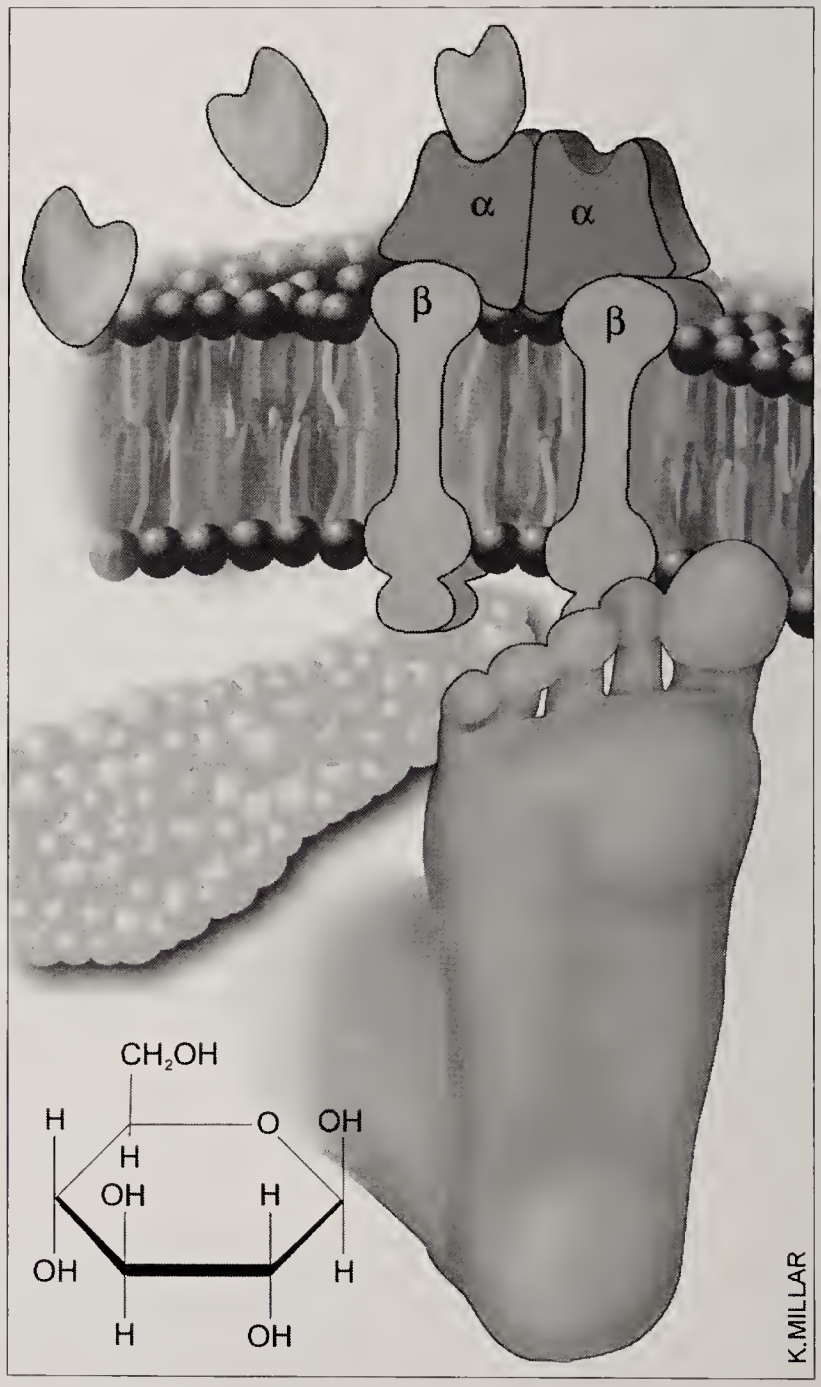
Ann Bugeja, B.Sc. (OT1), and Joseph Azzopardi,* MD (Malta), MRCP (UK), FRCP (Edin), FRCP (Lond)

Abstract

The elucidation of factors affecting the extended length of stay (LOS) of patients in a general medical ward allows for the assessment of hospital care and directs efforts to improve resource utilization in the treatment of diabetic patients. The special interest of the general medical ward studied is in Diabetes Mellitus. Inpatient data forms outlining the nature of the patients' admission for 160 discharged patients were completed. The average length of stay of patients on a general medical ward was 9.4 (0.9 days with a median of 7 days. 7.5% of patients had a LOS greater than 18 days and these patients occupied 34 percent of total bed days. This extended length of stay was largely due to patients with diabetic foot infection, social issues or neoplasm. The mean LOS of patients with a diabetic foot infection was 24 days (7.3 days with a median of 11 days. Patients with a diabetic foot infection (7) occupied 11% of bed days. A two-sample t-test showed a significant difference ($p<0.05$) between the average length of stay of patients with a diabetic foot infection and all other patients. These results suggest that alternative methods of resource utilization and optimization must be considered in the treatment of patients with a diabetic foot infection.

Introduction

St. Luke's Hospital is the main acute care hospital in Malta and, like all teaching hospitals, is challenged by the need to deliver quality health care in the context of fiscal constraints. Management of this problem involves the consideration of



Kevin Millar

* Consultant Physician and Head of the Department of Medicine, University of Malta

resource utilization. Analysis of the length of stay of inpatients can direct attention to those who stay longest in hospital. It follows that those who stay longest in hospital utilize the most resources available to inpatients. Is this resource allocation justified in the provision of optimal care?

The frequency of particular diagnoses is also a marker for resource utilization. Upon identification of these groups, each group can be carefully analyzed for in-group differences. For example, why do some patients remain in hospital longer than others for diabetic ketoacidosis?

The analysis of the length of stay of inpatients targets the need for progression in the prevention and treatment of certain medical conditions. Diabetes mellitus is a medical condition that requires such consideration.

Abnormalities in glucose tolerance are a major public health problem in Malta.[1] In 1981 a nationwide study regarding the prevalence of abnormalities in glucose tolerance was conducted in individuals aged 15 years and over.[1] The prevalence of diabetes and of impaired glucose tolerance were found to be 7.7% and 5.6%, respectively.[1] Abnormalities in glucose tolerance increased with age from 35 years onwards.[1] While, the prevalence of diabetes mellitus was found to be higher in females, a slightly higher prevalence of impaired glucose tolerance was found in males.[1]

Diabetes mellitus and its complications account for a large proportion of hospitalizations and hospital costs.[2] Diabetic foot problems account for more hospital inpatient days than do any other diabetic problems.[3] Diabetic neuropathy and peripheral vascular disease are the main etiologic factors in foot ulceration and may both lead to foot deformity and increased susceptibility to infection. Ulcers, the most common type of wound in diabetics,[4] allow an avenue for infection and they can cause progressive tissue necrosis and poor wound healing in the presence of ischemia.[5] Therefore, foot ulceration can lead to lower extremity amputation.[5,3]

Inpatient admissions and outcomes were documented to analyze the length of stay of hospital patients, to analyze resource utilization and to identify the need for changes in health care delivery. Attention was focused on patients with diabetes because of the unit's special interest in this condition and the high prevalence of diabetes in hospitalized patients.

Method

Inpatient data forms were utilized to prospectively track 160 patients discharged from under the care of a particular consultant (a diabetologist). Age, sex, referral source, number of admissions under present consultant, primary diagnosis, concomitant illnesses, special physical findings, abnormal laboratory results, length of hospital stay, and destination upon discharge were obtained and documented.

The referral source implies whether the patient was referred for admission by a general practitioner (either by a physician in a public health clinic or in private practice), by a diabetologist in the outpatient diabetes clinic or by self-referral. Concomitant illnesses are documented by primary, secondary, tertiary, and quartenary diagnoses (as per the discharge letter). Destination upon discharge refers to whether the patient was going home, going to an institution (a rehabilitation centre, nursing home or mental hospital) upon discharge or had died.

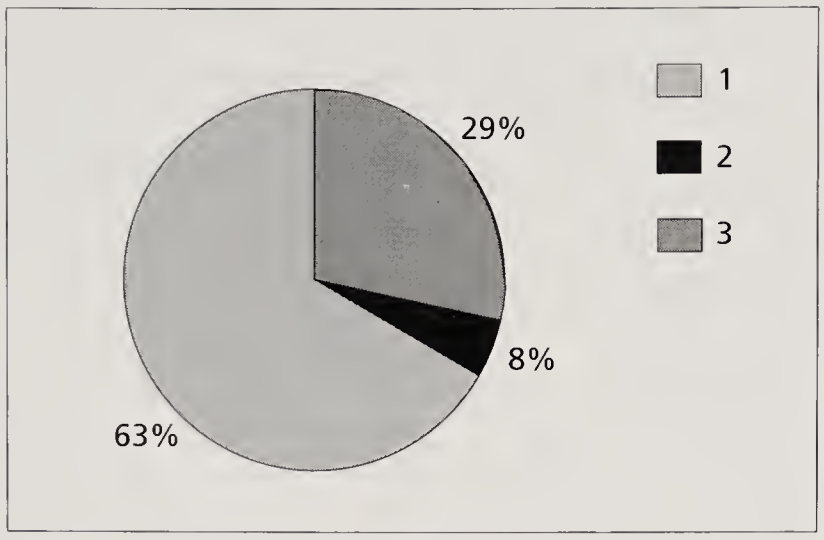


Figure 1. *Pie graph displaying distribution of referral source. 1: Primary Care Physician; 2: Self-referred; 3: Outpatient Clinics.*

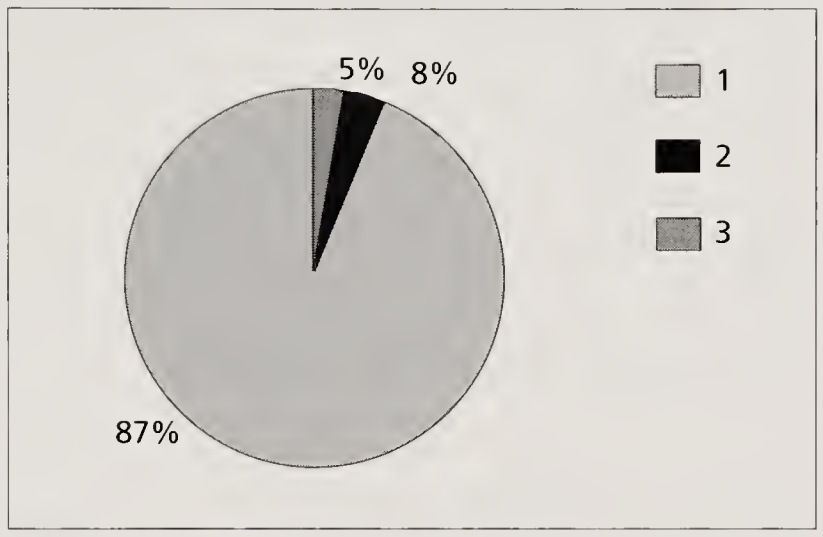


Figure 2. *Pie graph displaying destination upon discharge. 1: Home; 2: Institution; 3: Deceased.*

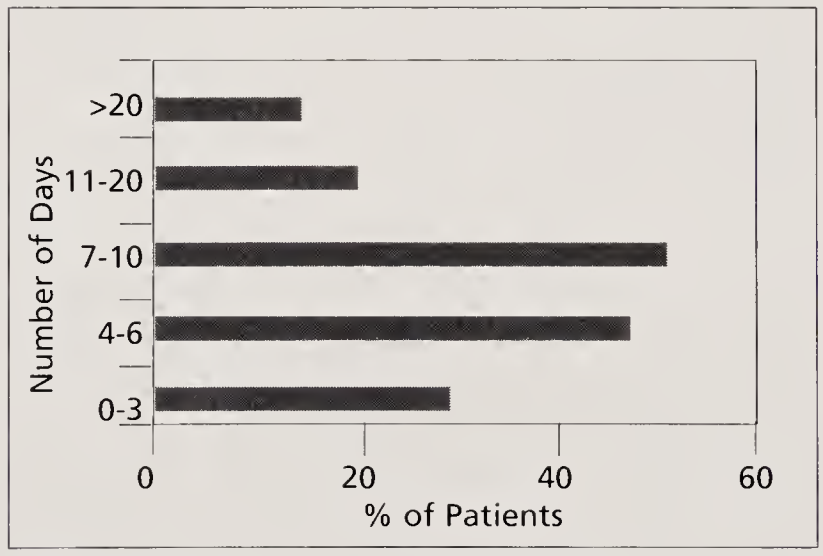


Figure 3. *Distribution of the length of stay in hospital.*

Table 1
Frequency of Primary Diagnoses

Specific Diagnosis	# of Diagnoses	% of Diagnoses
Asthma/COAD	7	4
Atypical Chest Pain	10	6
Cardiovascular	50	30
Cerebrovascular	6	4
Diabetes mellitus	30	18
Infection	24	15
Neoplasm	8	5
Other	30	18
Total	**165**	**100**

Table 2
Diagnoses of Diabetes Mellitus by Complication

Specific Diagnosis	# of Diagnoses	% of Diagnoses
Diabetic Ketoacidosis	10	33*
Diabetic Foot Infection	7	23*
Uncontrolled DM	13	43*
Hyperosmolar Coma	0	0
Total	**30**	**100**

**Rounded to nearest whole number.*

Table 3
Diagnoses - Cardiovascular

Specific Diagnosis	# of Diagnoses	% of Diagnoses
Angina	11	22
Arrhythmias	8	16
Heart Failure	11	22
Ischaemic Heart Disease	7	14
Myocardial Infarction	13	26
Total	**50**	**100**

The patients were located primarily on two general medical wards where nurses were experienced in the care of diabetic patients. For example, these nurses were familiar with the specific protocol outlined for the treatment of diabetic ketoacidosis and with foot ulceration treatment. Patients transferred between wards (e.g., from the coronary care unit to the general medical ward) were tracked as well.

The same person (A.B.) completed all forms upon the discharge of patients.

Results

One hundred and sixty patients were discharged and 160 inpatient data forms were consequently completed from June 1998 to August 1998. Seventy-five discharged patients were female and 85 discharged patients were male. A primary care physician (Figure 1) referred the majority of inpatients. Eighty-seven percent of inpatients were discharged home, 8% of inpatients were discharged to an institution (elderly home or rehabilitation centre) and 5% died while in hospital (Figure 2). Figure 3 illustrates the utilization of hospital beds by length of stay. Table 1 describes the frequency of primary diagnoses. Table 2 is a breakdown of the primary diagnosis Diabetes mellitus by complication. Table 3 is a breakdown when the primary diagnosis was Cardiovascular.

The length of stay of patients was studied. The average length of stay of patients on a general medical ward was 9.4 (0.9 days with a median of 7 days. 7.5% of patients had a LOS greater than 18 days and these patients occupied 34 percent of total bed days. The average length of stay among the 12 patients whose length of stay was greater than 18 days, was 43 (5.3 days. This extended length of stay was largely due to patients with a diabetic foot infection, neoplasm, or social issues.

The mean LOS of patients with a diabetic foot infection was 24 days (7.3 days with a median of 11 days. Patients with a diabetic foot infection[7] occupied 11% of bed days. The first and third quartiles were 9 and 39 days respectively. A two-sample t-test showed a significant difference ($p<0.05$) between the average length of stay of patients with a diabetic foot infection and all other patients.

Length of stay was analyzed for the two diagnoses*: diabetes and infection. The mean LOS was compared between age groups (50 and >50 years of age for each diagnosis. The analysis was performed using t-tests (assuming unequal variances). There was a significant difference among the two age groups ($p<0.05$) for the diagnosis of infection.

A strong correlation of 0.98 was found between age and LOS for patients whose primary diagnosis was diabetes mellitus. A two-sample t-test showed a significant difference ($p<0.005$) in the ln(LOS) of the two different age groups; patients age >50 had a significantly longer length of stay in hospital. The mean LOS of the two age groups was also compared for the specific diagnosis of diabetic ketoacidosis (DKA). Patients in the age group >50 years of age remained in hospital longer than those who are (50 years of age ($p < 0.01$).

Discussion

It is not clear whether reducing the number of beds available will result in an improved turnover per available bed or lead to more discretionary admissions rather than differences in the length of stay.[6] Attention needs to be focused on appropriate resource utilization in the management of patients who remain longest in hospital and on medical conditions that require a large proportion of hospital bed days.

* Note: An analysis of the cardiovascular diagnoses could not be performed because three diagnoses were in patients <50 years of age.

One way to decrease the length of stay of patients with social issues is the use of a case management program.[7] The role of the case manager (a nurse or other health care professional) is to assess patients at admission to identify potential problems with the discharge process and to contact the appropriate services necessary (e.g., social services, intravenous therapy, home health care). The case manager participates in daily rounds to obtain current patient information, identify deficiencies in health maintenance, and advise regarding discharge planning. The case manager also justifies resource utilization and facilitates discharge planning. Contact is maintained with patients and families after discharge regarding follow-up appointments and changing health status. This case management program was effectively implemented in a teaching hospital on a general medicine ward.[7]

Patients with a diabetic foot infection also remain longer in hospital. Six percent of diabetic patients admitted to the hospital annually in the U.S. are admitted because of a foot ulcer. 8 Foot problems were found to be responsible for 23 percent of the hospital days over a period of 2 years.[8] Diabetic foot infections accounted for 11 percent of bed days at St. Luke's Hospital. Patients with a diabetic foot infection remain longer in hospital and efforts are needed to reduce the length of stay of nonacute care patients staying in acute care hospital beds. The costs associated with a diabetic foot infection are well documented.5 Alternative methods of management of diabetic foot lesions include intravenous antibiotic therapy for 48 hours until culture results available followed by appropriate oral antibiotic therapy at home,[5,9,10] as well as home intravenous therapy.[11] These alternatives can produce significant cost savings in appropriately selected patients.[11] However, potential problems exist for these therapeutic options when implemented in the home setting. Selection of the 'appropriate' patients is problematic in itself. Home therapy is not useful if patients remain on their feet at home which is likely if the patient has obligations and responsibilities to others or lack of social support. In face of these considerations, it is appropriate to assign hospital beds for patients with diabetic foot problems - to focus on saving feet from further complication. This will allow for specialized attention on a subacute medical problem with availability of acute beds to care for other patients. Therefore, all patients will receive better care by the diabetic team with more appropriate resource utilization.

Other in-hospital treatments can also be considered in the context of allotting beds for diabetic patients with foot infection. Granulocyte-colony stimulating factor (G-CSF) therapy for one week was associated with earlier eradication of pathogens from the infected ulcer (mean 4 versus 8 days), quicker resolution of cellulitis (7 versus 12 days), shorter duration of intravenous antibiotic treatment (8 versus 14 days), and shorter duration hospital stay (10 versus 18 days) when compared with placebo.[12]

Furthermore, two other strategies will act synergistically with bed space assigned for patients with diabetic foot problems: patient education and foot inspection. Foot inspection must be done on a daily basis by the patient and a nurse and/or physician should inspect and review foot care with the patient during every visit.[5,13] Instructions must be explained and questions should be encouraged so that the patient can attain a better understanding of the importance of foot care. Time must be taken to discuss footwear and the implementation of such instructions in the context of the patient's daily routine; i.e. the program must be tailored to the life of each individual patient. Proper education and inspection will prevent diabetic foot problems and secondarily reduce the hospital admissions for diabetic foot infection. Aggressive educational strategies can also be implemented for the care of all diabetic patients. These educational tools will reduce the accumulation of diabetic complications over time that cause older patients to remain longer in hospital for similar diagnoses like DKA.

The limitations of the study include a small sample size due to the restricted length of study and an absence of statistical evidence of the length of stay of patients on a general medicine ward from 10 years ago. Therefore, this study provides a baseline for future analysis. Further research can then be elicited to evaluate educational practices in the future by analzying outcomes: are there less diabetic complications in elderly diabetic patients? Are there any changes in the prevalence of diabetic foot infections and the length of stay of these patients in hospital that are attributable to these educational processes?

Acknowledgements

We thank the following people for their help and support of the project: Dr. M. Cacchia, Dr. S. Fava, Dr. J. Vassallo, Dr. A. Falzon, and Dr. R. Micallef. We also thank Mid-Med Bank and Bank of Valletta for their interest and financial support.

References

1. Schranz AG. (1997). The Epidemiology of Diabetes in Malta. *Diabetes/Metab. Rv.* 13(3):181-199.
2. Levetan CS, Salas JR, Wilets IF, et al. (1995). Impact of Endocrine and Diabetes Team Consultation on Hospital Length of Stay for Patients With Diabetes. *Am. J. Med.* 99(1):22-28.
3. Shaw JE, Boulton AJM. (1997). The Pathogenesis of Diabetic Foot Problems: An Overview. *Amer. Diab. Assoc.* 46(2S)Supplement:58S-61S.
4. Lavery LA, Armstrong DG, Vela SA *et al.* (1998). Practical Criteria for Screening Patients at High Risk for Diabetic Foot Ulceration. *Arch. Intern. Med.* 158(2):157-162.
5. Levin M. (1995). Preventing Amputation in the Patient With Diabetes. *Diabetes Care.* 18(10):1383-1394.
6. Sudell AJ, Horner JS, Jolly U, *et al.* (1991). Length of stay in general medical beds; Implications for the NHS White Paper of variance within one performance indicator. *Journal of Public Health Medicine.* 13(2):88-96.
7. Sivaram CA, Attebery S, Boyd AL, *et al.* (1997). Introducing Case Management to a General Medicine Ward Team of a Teaching Hospital. *Acad. Med.* 72:555-557.
8. Smith DM, Weinberger M, Katz BP. (1987). A controlled trial to increase office visits and reduce hospitalizations of diabetic patients. *J. Gen. Intern. Med.* 2:232-238.
9. Black J, Hunt TL, Godley PJ, *et al.* (1987). Oral antimicrobial therapy for adults with osteomyelitis or septic arthritis. *J. Infect. Dis.* 155:968.
10. Mader JT, Cantrell JS, Calhoun J. (1990). Oral ciprofloxacin compared with standard parenteral antibiotic therapy for chronic osteomyelitis in adults. *J. Bone Joint Surg.* 72:104.
11. Fox HR, Karchmer AW. (1996). Management of diabetic foot infections, including the use of home intravenous antibiotic therapy. *Clin. Podiatr. Med. Surg.* 13(4):671-682.
12. Gough A, Clapperton M, Rolando N, *et al.* (1997). Randomised placebo-controlled trial of granulocyte-colony stimulating factor in diabetic foot infection. *Lancet.* 350:855.
13. Wylie-Rosett J, Walker EA, Shamoon H, *et al.* (1995). Assessment of Documented Foot Examinations for Patients With Diabetes in Inner-city Primary Care Clinics. *Arch. Fam. Med.* 4(1):46-50.

Office of **S**tudent **A**ffairs

Faculty of Medicine, University of Toronto

Here to **MATCH** Your Needs

PERSONAL	• crisis/problems • health (physical and emotional) • safety/security • mistreatment in personal/academic life • housing and other issues of concern
ACADEMIC	• mentors • leave of absence/withdrawal from school • special accommodations for disabilities
CAREER	• Glaxo Career Pathway Program • career fairs • licensing examinations, etc. • skills for interviews, resume and letter writing
BRIDGING THE GAP	• stress and time management • study skills • gender and equity issues • multicultural issues • other pertinent concerns and issues raised by students

In the spirit of the medical profession,
all personal counselling is done discreetly

Associate Dean: Dr. Miriam Rossi

Coordinator: Ms. Diana Alli

Medical Sciences Building
Rm. 3245
1 King's College Circle
Toronto, Ontario
M5S 1A8
(416) 978-2764

P.A.S.S.

Program for Advice and Support for Students

Faculty of Medicine, University of Toronto

A **confidential** support program for medical students separate from the Dean's Office.

Academic Concerns	—	problems keeping up with studies
	—	failing a course
	—	concern about teachers, etc.
Personal Concerns	—	self confidence, relationships, family problems, stress
Social Concerns	—	sexism, racism and social responsibility of Medical School
Resource Centre	—	pamphlets, brochures and books available
Workshops/Seminars	—	These can be arranged where students feel there is an issue of general interest (choosing a specialty, financial management, starting a family, etc.)

Twelve Advisors from Clinical and Basic Sciences – 24 hour availability.

Referrals to special services at the University, Hospitals or in the Community.

The PASS Office is located in Room 2263, Medical Sciences Building – Telephone 978-1177
Director: Dr. Niall Byrne; Administrator: Katherine Harris.

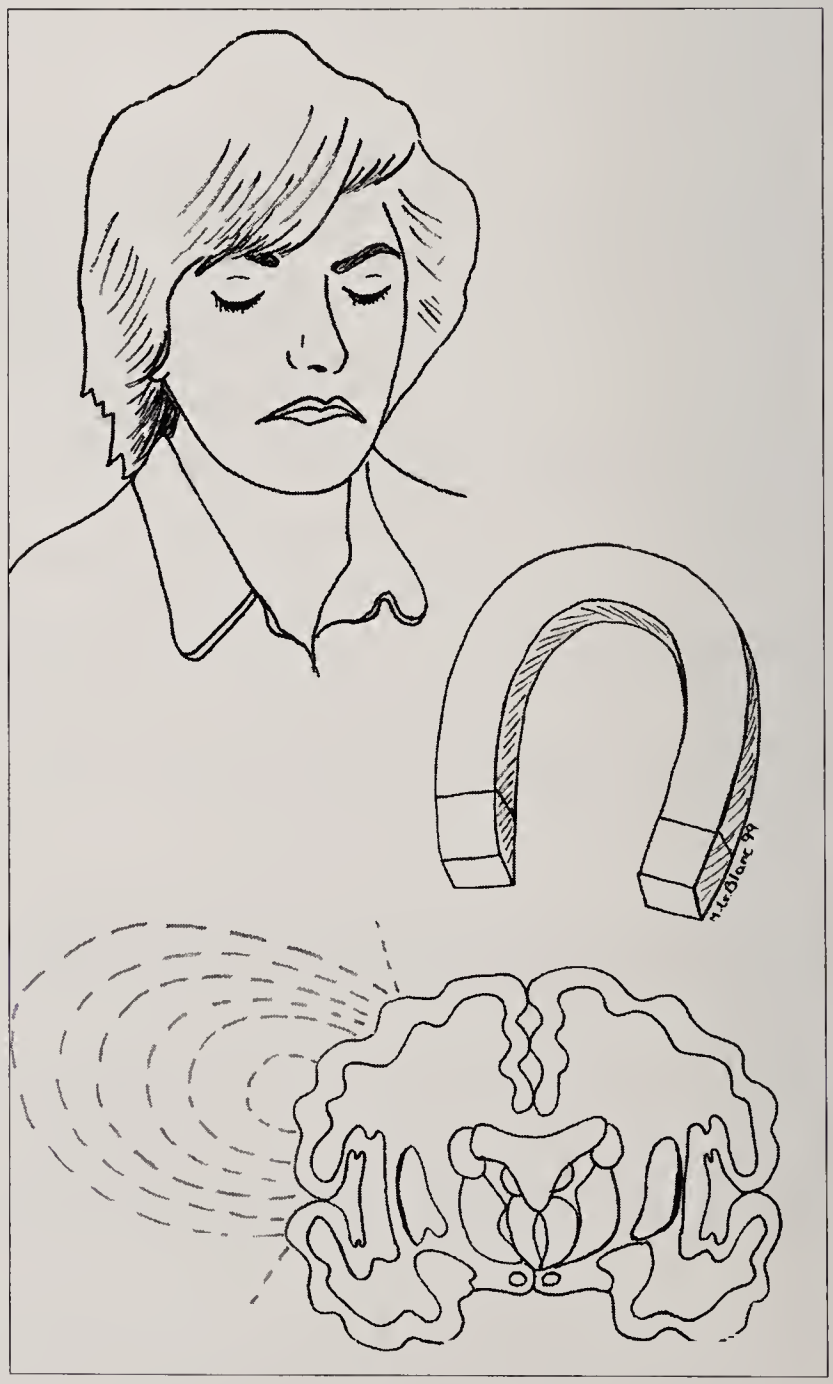
DROP IN ANY TIME DURING OFFICE HOURS
APPOINTMENTS NOT NECESSARY

An Introduction to Transcranial Magnetic Stimulation and Its Use in the Investigation and Treatment of Depression

Dan Mozeg, BSc., (OTO), and Edred Flak, MD, FRCP(C)

Abstract

Research during the past decade and a half has led to the development of Transcranial Magnetic Stimulation (TMS). In this procedure a pulsed magnetic field generated extracranially induces focal intracranial electrical discharges. TMS has been used in the investigation of neurological and neuropsychiatric disorders, and more recently has emerged as a tool in the study and treatment of depressed mood in the context of Major Depressive Disorder and Bipolar Disorder. Although data are limited and preliminary, early results are promising with regards to the efficacy of TMS in alleviating depressed mood. The antidepressant effect, however, is currently short-lived, lasting hours to weeks. TMS appears to be safe, with only minor side effects in both healthy and neurologically impaired individuals. However, a possible increased predisposition to generalized seizures may exist among those with multiple sclerosis, stroke, and epilepsy, both during and following the procedure. Ongoing research into optimization of hardware specifications, treatment protocols, and side-effects, may allow TMS to emerge as an alternative to psychoactive medications and electroconvulsive therapy in treating primary psychiatric disorders where depressed mood is prominent, as well as secondary and reactive depression arising in the context of medical conditions and surgical procedures.



Monique LeBlanc

Transcranial Magnetic Stimulation – An Introduction

Following the discovery of the unified and interchangeable nature of electric and magnetic forces, it became evident that electric currents generate magnetic fields while changing magnetic fields generate electric currents. By this time it

had already been well established by Galvani's and Volta's classic experiments that electric currents were capable of stimulating neuronal tissues. The combination of these two concepts – the unity of electric and magnetic forces, and the responsiveness of neurons to electrical stimulation – is now being harnessed to study and manipulate the central nervous system (CNS) from both neurologic and psychiatric perspectives. A technique called Transcranial Magnetic Stimulation (TMS) uses an externally generated changing magnetic field to induce electric current intracranially. This is in contrast to the application of an electric current that is generated externally and transmitted to the brain through the skull (for example in electroconvulsive therapy). When electricity is forced to pass through the skull, the current used must be relatively large as the skull is a powerful insulator with an electrical resistance 8 to 15 times greater than that of soft tisues.[2] Furthermore, externally generated electric currents cannot be focally directed as the skull dissipates the electricity globally leading to massive depolarization of cortical and subcortical structures.[2] Such difficulties are minimized upon exposure of the skull to TMS, where the changing external magnetic field undergoes minimal attenuation in the skull tissues while inducing smaller, focally directed electric currents within the brain.[1,2]

Barker *et. al.* first described in 1985 the use of a pulsed (i.e. changing) magnetic field focused over specific regions of the cerebral cortex to induce muscle action potentials.[3,4] The use of pulsed magnetic fields to induce electrical activity in peripheral nerves had been described much earlier, in the 1960's.[1] The mathematical framework describing how pulsed magnetic fields may be used to generate electrical currents in the human brain was subsequently described by Barker in 1987.[1] The technique requires a hand-held coil shaped as a circular disc (or more recently as a figure-8), with an inner diameter of approximately 60 millimeters (mm) and an outer diameter of approximately 130mm. The coil is held near the patient's head, and is connected to a power-source which generates an electric current that is switched on and off repeatedly producing a changing magnetic field in the vicinity of the coil. The frequency at which the current (and hence magnetic field) is pulsed varies from as low as 1-5 Hz to as high as 25-30 Hz. The higher frequency technique has been found to be particularly effective in psychiatry and has been termed Rapid Rate Transcranial Magnetic Stimulation (rTMS).[1,5,6] rTMS is believed to be unique in that rapid pulsation can induce electrical currents within neurons while they are in the refractory period, although how this relates to an altered clinical manifestation is unclear. The magnetic field, passing largely unimpeded through the skull, induces a current within the brain tissue.[1] Depending on the region of the brain over which the coil is physically placed, specific circumscribed areas can be stimulated. This avoids generalized seizure-like discharge and global stimulation of cortical and subcortical structures.

TMS has been used for multiple purposes in the field of neurology including establishing hemispheric language dominance, localization of epileptogenic foci, and the study of motor pathways originating at the cerebral cortex and relevant motor pathway physiology.[1,2,6,7] It has also been utilized in neuropsychiatry in the mapping of attention, memory, movement, speech, and vision.[8] Clinically, TMS has been combined with electromyographic studies (EMG) to determine impairment in CNS conduction pathways by measuring differences in the rates of muscle activation upon electromagnetic stimulation at the cerebral cortex in comparison with similar stimulation at spinal nerve roots.[1,9,10] This assessment is useful in the diagnosis and prognostication of demyelinating diseases such as multiple sclerosis. More recent efforts have focused on the use of TMS in the symptomatic improvement of Parkinson's disease.[9,11,12]

Being a relatively new technique, optimization of parameters such as frequency of pulsing of the magnetic field, size of the coil utilized, strength of the magnetic field generated, and duration of induction of electrical current has yet to be established.[13,14] Furthermore, it is likely that such parameters will vary substantially depending on the specific neurological or psychiatric applications.

Use of TMS in the Treatment of Primary Mood Disorders

Several serendipitous findings in the course of neurological and psychoneurological testing have suggested that TMS may be useful in the study and treatment of primary psychiatric mood disorders. Grisaru *et. al.* noted an improvement in the mood of two Parkinsonian patients following TMS while measuring nerve conduction times, while studies of hemispheric language dominance using rTMS have found affective reactions in a considerable number of patients following dominant frontal cortex stimulation.[7,15,16] Given that TMS is focally applied, however, the question arose as to which specific regions of the brain should be stimulated. Dysfunction in the frontal lobes, particularly involving the left prefrontal cortex, has been implicated in the development of major depressive episodes.[13,17,20] Furthermore, studies of patients with strokes causing damage in the left prefrontal cortex have suggested an increased risk of developing depression, while studies of patients with multiple sclerosis have shown a greater number of plaques in the left frontal lobe of those who have comorbid depression in comparison to patients with similarly severe multiple sclerosis but no depression.[17,20] Findings from functional neuroimaging studies, Computed Tomography, and Magnetic Resonance Imaging have also described abnormalities in the left prefrontal cortex in both primary and secondary depression.[17,19] The observation that TMS may affect mood states, and the implication of the frontal lobes in the pathogenesis of depression have led investigators to examine the efficacy of TMS applied to regions of the frontal cortex in studying

and treating depression arising in the context of Major Depressive Disorder (MDD) and Bipolar Disorder (BD).[13,17,18]

George *et. al.* in 1995 reported an open study of six patients with treatment resistant depression, who were subjected to rTMS of the left prefrontal cortex over the course of one week.[17] All patients had primary mood disorders, five being BD type II and one suffering from MDD. All were in the midst of a major depressive episode. For the group as a whole a significant improvement in mood was noted, with a decrease in the mean Hamilton Depression Rating Scale score from 23.8 to 17.5 on the 17-item scale.

Pascual-Leone *et. al.,* in 1996, described a multiple cross-over, randomized, placebo-controlled trial studying rTMS stimulation of the left dorsolateral prefrontal cortex in drug resistant depression.[13] Seventeen patients with MDD, multiple relapses of major depressive episodes, and psychotic features were studied. The patients received 5 courses of TMS, each lasting five days. These included real left frontolateral TMS, real right frontolateral TMS, placebo TMS of these two regions, and real TMS of the mid-frontal region. Both the Hamilton Depression Rating Scale and the Beck Depression Inventory were used to assess depressed mood at baseline and following treatment. Nine of the patients were found to experience improvement in mood only following administration of real left frontolateral TMS, while three patients reported improvement in mood following both administration of left frontolateral and mid-frontal TMS. Two patients reported subjective improvement in mood following only real left and real right frontolateral TMS. In all patients the lowest Beck and Hamilton scores (i.e. least depressed mood) followed administration of left frontolateral TMS, and represented a statistically significant improvement over baseline. TMS stimulation of all other areas of the brain demonstrated no statistically significant improvement (and at times an increase) in Hamilton and Beck scores versus baseline. The average duration for which patients reported a significant improvement in mood following left frontolateral TMS was limited to 2 weeks following cessation of stimulation of this area.

Pascual-Leone *et. al.* studied 10 healthy volunteers and assessed subjective perception of five emotional domains on visual analogue scales.[20] These domains included "happiness", "anxiety", "tiredness", "pain and discomfort", and "sadness". TMS was applied over the course of 3.5 hours, with 5 minute sessions and 30 minute intervals between sessions. After each session participants were required to fill in the five analogue scales, noting the intensity of each of the above emotions. The TMS sessions involved right prefrontal, left prefrontal, and mid-frontal regions, applied in varying order to correct for possible sequential effects of the treatment. The authors concluded that no clinically apparent mood changes were evoked by rTMS applied to any scalp position when compared to baseline. However, left prefrontal TMS did result in a significant increase in the "sadness" rating on the visual analogue scale, and a significant decrease in the "happiness" rating when compared to the right- and mid-prefrontal regions.

George *et. al.* also demonstrated a lateralization in their study of 10 healthy volunteers, although left prefrontal stimulation was again found to be associated with a worsening of mood.[21] After applying rTMS to the right, left, and mid-frontal corteces, as well as to the occipital and cerebellar regions, left prefrontal stimulation was found to be associated with an increase in self-rated feelings of sadness, while right prefrontal stimulation was found to be associated with an increase in self-rated feelings of happiness.[21] The results of these two studies are inconsistent with the previously described studies which showed improvement in mood when the left prefrontal cortex was stimulated. The difference may stem from variability in the physical parameters and settings of the TMS equipment, and the protocol used. Furthermore, these two latter studies assessed healthy patients over the course of hours while the previously described two studies assessed pathologically depressed patients over the course of several weeks. This raises the possibility that TMS may impact differently on healthy individuals as compared to those who are depressed. It is worth noting that all studies implicate the frontal lobes as important in the maintenance of mood states and point to a lateralization of mood within them.

Assessment of the value of TMS in the management of mood disorders has also been attempted within the context of laboratory models. Fleischmann *et. al.* in 1995 described the effects of TMS on rat brains in behavioural models of depression.[18] Their findings suggested that TMS had neurological and behavioural effects similar to those induced by electroconvulsive shocks.

Safety of TMS

Barker *et. al.,* describing TMS in its early days, believed this technique to be relatively safe.[1] They calculated the amount of thermal energy deposited in tissues as a result of the procedure to be very small. They described the peak magnetic field used in the procedure as being similar in magnitude to the static fields used in magnetic resonance imaging scanners, and noted that no adverse effects had yet been attributed to such magnetic fields. Consistent with this view is the report by Pascual-Leone *et. al.,* whereby none of the seventeen patients in their study reported adverse effects other than minor headaches which were relieved with mild analgesics.[13] Bridgers and Delaney assessed 30 healthy adults for cognitive and motor performance following TMS.[22] No statistically significant declines in story recall, word association, visual recall, or grip strength were observed. A study of 9 normal volunteers by Pascual-Leone *et. al.* found that

rTMS was not associated with significant changes in neurological examination findings, cognitive performance, EEG, electrocardiogram, or levels of anterior pituitary hormones.[23] However, the highest intensity stimulus of TMS did produce a focal seizure in one patient, which secondarily became generalized. Chokroverty *et. al.* concluded that TMS was not associated with any apparent deleterious effects in the short term and in long term follow-up of 16 to 24 months, after assessing EEG data, psychometric test results, anterior pituitary hormone levels, and onset of fatigue in normal subjects undergoing this procedure.[24] Transient decline in delayed recall was noted, resolving 2 weeks after the procedure.

Several authors raised the possibility of seizure induction during or following TMS in healthy subjects and in those with neurological conditions such as epilepsy and stroke.[2,25,26,27,30] The majority of reports, however, have been anecdotal. Others contend that TMS is a safe procedure in both healthy and neurologically impaired persons. Kandler reports on a 3 to 21 month post-TMS survey sent to patients with multiple sclerosis, Parkinson's disease, or stroke, assessing various aspects of physical health.[28] Of 133 patients who responded, only one experienced a single seizure and another experienced two seizures in the month following TMS (both had multiple sclerosis). The only other side effects noted by Kandler were headache in five respondents, and transient memory loss in three. Homberg *et. al.,* while describing their experiences with a patient who developed a seizure during a course of TMS, note that this patient may have represented a unique subgroup having a large ischemic scar following a middle cerebral artery infarction.[26] They suggest that the risk of epileptic seizures in most individuals is low, even in patients with previously known epilepsy or stroke. They also note that in approximately 2000 TMS examinations over the course of 2 years at the National Hospital for Nervous Diseases in London, England, no seizures occurred. Tassinari *et. al.* report on a study of 58 patients with partial or generalized epilepsy who had transcranial magnetic stimulation (TMS) of the brain motor regions.[31] Short-term monitoring demonstrated that stimulation did not provoke seizures or EEG changes in any patient, and long-term follow-up showed that the epileptic condition was not made worse by TMS. Their conclusion was that TMS, at least as used for monitoring conduction in central motor pathways, does not induce seizures in drug-treated epileptic patients. Gates *et. al.* assessed histopathalogically the temporal lobes of two patients who received TMS and subsequently underwent lobectomy for medically intractable epilepsy two or four weeks following TMS.[32] They concluded that no lesions were attributable to TMS in these specimens.

Conclusion

TMS is a relatively new technique, currently standing at the threshold between experimental investigation and clinical application. It holds prospects as both a research tool and a therapeutic modality in psychiatric mood disorders. Reports of the effectiveness of TMS in treating depression are limited, however, and most are either anecdotal or open-study based with small heterogeneous sample sizes. Furthermore, no studies have directly compared TMS to conventional therapies. Therefore, replacement by TMS of antidepressant medication in MDD, mood stabilizers in BD, or ECT in both of these conditions, cannot be advocated. Moreover, the effects of TMS currently appear to be short-lived, necessitating frequent repetition of the treatment. Further investigation and refinement of the equipment and treatment protocols, and more detailed and well controlled studies are required before TMS may be considered for routine clinical use. This is evident in the variability of treatment protocols reported in the literature, and in the uncertainty regarding the optimal parameters to use. Nevertheless, this technique opens a new frontier in mood disorder research and patient management, and provides impetus for further investigation into novel methods of managing these often complex conditions. TMS appears to be a safe procedure, particularly among those individuals with no previous neurological conditions. Therefore, its ongoing use in this population for the purposes of further investigation and preliminary treatment efforts appears justified. Even among those with a history of neurological conditions such as multiple sclerosis, epilepsy, and stroke, TMS appears to be safe and these conditions do not as yet pose an absolute contraindication to the procedure. Given the reports of seizure induction in these patients, however, further study and cost-benefit assessment are required before routine use can be advocated. The applications of TMS may not be limited to primary mood disorders. Other psychiatric conditions where mood symptoms are prominent, such as schizophrenia, schizoaffective disorder, and post-traumatic stress disorder, may respond to the procedure. Furthermore, TMS may prove useful in the management of reactive depression arising in the context of a multitude of medical illnesses and surgical procedures.

References

1. Barker AT, Freeston IL, Jalinous R, Jarrat JA. (1987). Magnetic stimulation of the human brain and peripheral nervous system: An introduction and the results of an initial clinical evaluation. *Neurosurgery.* 20:100-109.
2. Dhuna A, Gates J, Pascual-Leone A. (1991). Transcranial Magnetic Stimulation in patients with epilepsy. *Neurology.* 41:1067-1071.
3. Barker AT, Freeston IL, Jalinous R, *et. al.* (1985). Magnetic stimulation of the human brain. *J Physiol.* 369:3P.
4. Barker AT, Jalinous R, Freeston IL. (1985). Non-invasive magnetic stimulation of the human motor cortex. *Lancet.* 1:1106-1107.
5. McCann UD, Kimbrell TA, Morgan CM, *et. al.* (1998). Repetitive Transcranial Magnetic Stimulation for post traumatic stress disorder. *Archives of General Psychiatry.* 55:276-279.
6. Pascual-Leone A, Valls-Solc J, Wassermann EM, Hallett M. (1994). Responses to rapid-rate Transcranial Magnetic Stimulation of the human motor cortex. *Brain.* 117:847-858.
7. Pascual-Leone A, Gates JR, Dhuna A. (1991). Induction of speech arrest and counting errors with rapid-rate Transcranial Magnetic Stimulation. *Neurology.* 41:697-702.
8. George MS, Wassermann EM, Post RM. (1996). Transcranial Magnetic Stimulation: a neuropsychiatric tool for the 21st Century. *Journal of Neuropsychiatry and Clinical Neurosciences.* 8:373-382.
9. Belmaker RH, Fleischann A. (1995). Transcranial Magnetic Stimulation: A Potential New Frontier in Psychiatry. *Biological Psychiatry.* 38:419-421.

10. Abarbanel JM, Lemberg TL, Yaroslavski U. *et. al.* (1996). Electrophystological responses to transcranial magnetic stimulation in depression and schizophrenia. *Biological Psychiatry.* 40:148-150.
11. Pascual-Leone A, Valls-Sole J, Brasil Neto JP, *et. al.* (1994). Akinesia in Parkinson's Disease, Part 1: Shortening of simple reaction time with focal, single pulse TMS. *Neurology.* 44:884-891.
12. Pascual-Leone A, Valls-Sole J, Brasil Neto JP, *et. al.* (1994). Akinesia in Parkinson's Disease Part 2; Effects of sub-threshold repetitive transcranial motor cortex stimulation. *Neurology.* 44:892-898.
13. Pascual-Leone A, Rubio B, Pallardo F, Catala MD. (1996). Rapid-rate Transcranial Magnetic Stimulation of left dorsolateral prefrontal cortex in drug-resistant depression. *Lancet.* 347:233-237.
14. Zyss T, Krawczyk A. (1996). Magnetic brain stimulation in treatment of depression: the search for effective parameters of stimulation. *Psychiatria Polska.* 30:611-628.
15. Grisaru N, Yaroslavsky U, Abarbanel J, *et. al.* (1994). Transcranial Magnetic Stimulation in depression and schizophrenia. *Eur Neuropsychopharmacol.* 4:287-288.
16. Michelucci R, Valzania F, Passarelli D, *et. al.* (1994). Rapid rate Transcranial Magnetic Stimulation and hemispheric languahe dominance: usefulness and safety in epilepsy. *Neurology.* 44:1697-1700.
17. George MS, Wassermann EM, Wendol AW, *et. al.* (1995). Daily repetitive transcranial magnetic stimulation improves mood in depression. *Neuroreport.* 6:1853-1856.
18. Fleishmann A, Prolov K, Abarbanel J, Belmaker RH. (1995). The effect of Transcranial Magnetic Stimulation of rat brain on behavioural models of depression. *Brain Research.* 699:130-132.
19. George MS, Ketter TA, Post RM. (1994) Prefrontal cortex dysfunction in clinical depression. *Depression.* 2:59-72.
20. Pascual-Leone A, Catala MD, Pascual Pascual-Leone A. (1996). Lateralized effect of rapid-rate Transcranial Magnetic Stimulation of the prefrontal cortex on mood. *Neurology.* 46:499-502.
21. George MS, Wassermann EM, Williams WA, *et. al.* (1996). Changes in mood and hormone levels after rapid-rate Transcranial Magnetic Stimulation of the prefrontal cortex. *Journal of Neuropsychiatry and Clinical Neurosciences.* 8:172-180.
22. Bridgers SL, Delaney RC. (1989). Transcranial Magnetic Stimulation: an assessment of cognitive and other cerebral effects. *Neurology.* 39;417-419.
23. Pascual-Leone A, Houser CM, Reese K, *et. al.* (1993). Safety of rapid rate Transcranial Magnetic Stimulation in normal volunteers. *Electroencephalography and Clinical Neurophysiology.* 89:120-130.
24. Chotrovsky S, Hening W, Wright D, *et. al.* (1995). Magnetic brain stimulation: safety studies. *Electroencephalography and Clinical Neurophysiology.* 97:36-42.
25. Pascal-Leone A, Valls-Sole J, Brasil Neto JP, *et. al.* (1992). Seizure induction and transcranial magnetic stimulation. *Lancet.* 339:997.
26. Homberg V, Netz J. (1989). Generalized seizures induced by transcranial bagnetic stimulation of motor cortex. *Lancet.* 334:1123.
27. Wassermann EM, Cohen LG, Flitman SS, *et. al.* (1996). Seizures in healthy people with repeated "safe" trains of transcranial magnetic stimuli. *Lancet.* 347:825-826.
28. Kandler R. (1990). Safety of Transcranial Magnetic Stimulation. *Lancet.* 335:469-470.
29. Zyss T. (1994). Deep magnetic brain stimulation – the end of psychiatric electroshock therapy? *Medical Hypothesis.* 43:69-74.
30. Hufnagel A, Elger CE, Durwen HF, *et. al.* (1991). Induction of seizures by Transcranial Magnetic Stimulation in epileptic patients. *J Neurol.* 238:109-110.
31. Tassinari CA, Michelucci R, Forti A, *et. al.* (1990). Transcranial Magnetic Stimulation in epileptic patients: usefulness and safety. Neurology. 40(7):1132-3.
32. Gates JR, Dhuna A, Pascual-Leone A. (1992). Lack of pathologic changes in human temporal lobes after Transcranial Magnetic Stimulation. *Epilepsia.* 33(3):504-508.

WHITEHALL ROBINS
TREATING YOU WITH CARE®

Makers of

Advil®

Your #1 Analgesic Choice

Corrections

UTMJ Volume 76, No. 2 (page 94)
Post-Streptococcal Reactive Arthritis in Children: A Review of the Literature
Dr. Nina Birdi is a Staff Pediatric Rheumatologist at the Children's Hospital in Ottawa.

UTMJ Volume 76, No. 2 (page 115)
Breathless

Table 2
Percentage Probability of Underlying Pulmonary Embolism According to the Criteria of PIOPED Study

Scan Probability			"Non-Diagnostic"	
Normal/Very Low	Low*	Intermediate*	High	Clinical Suspicion
Low	2	4	16	56
Intermediate	6	16	28	88
High	0	40	66	96

** Low or intermediate scans are nondiagnostic.*

Source: BMJ 1997:314, pg.426,Table 1.

York Downs Pharmacy
3910 Bathurst St.
North York, ON

Tel: 416-633-2244
Outside of Toronto:
1-800-564-5020
Fax: 416-633-3400

San Pharmacy Limited

e-mail: san.pharmacy@sympatico.ca

San Total Health Pharmacy
5954 Highway 7
Markham, ON

Tel: 905-201-1770
Outside of Toronto:
1-888-993-3666
Fax: 905-201-1760

Alternative
Complementary

Mainstream

Integrated Medicine

We at *York Downs* and *San Total Health Pharmacies* are committed to Proactive Health Care. We believe that the integration of *Mainstream Medicine* and *Natural Complementary Medicine* has emerged and will benefit all.

Knowledge, lifestyle, spirituality, positive attitude, regular exercise are but a few areas towards self-help. We assist physicians and healthcare practitioners to help patients help themselves.

We provide for your patients custom-tailored medications which include:

- ✓ dosage adjustments
- ✓ flavour modifications
- ✓ reformulations to suit doctor-patient personal preferences
- ✓ injectables prepared in our class 100 clean room
- ✓ natural hormone replacement therapy
- ✓ guidance on potential interaction between herbs and prescription drugs

Vitamins • Minerals • Naturapathic • Homeopathic • Ayurvedic • Orthomolecular

Compounders of:

- Natural Hormone Replacement Creams, Ointments, Suppositories and Capsules
- Injectable Preparations including:
  - Procaine Buffered
  - Lidocaine Preservative Free
  - Male Impotence
  - Vitamins, etc.
- Inhalation Formulas
- Injectables
- Lip Balms
  - Anesthetic
  - Anti-Viral
  - Sunscreen
- Medical Lollipops
- Lotions
- Mouthwashes
- Non-Aerosol Sprays
  - Nasal
  - Oral
- Ointments
- Opthalmic Specialities
- Optic Insufflations
- Optic Solutions & Suspensions
- Pediatric Formulations
- Physical Therapy Formulations
  - Scalding Gels
  - Ionizing Solutions
  - Iontophoretic Formulations
  - Phonophoretic Fomulations
- Podiatric Formulations
- Popsicles
- Powders
- Capsules
  - Regular
  - Time-released
- Creams
  - Topical
  - Rectal
  - Vaginal
  - Disposal Applicators
- Dental Preparations
- Dermatological Specialities
- Discontinued Products
- Ear Drops
  - Solutions
  - Suspensions
- Enemas
- Eye Drops
  - Sterile
  - Preservative Free
- Gels
  - Topical
  - Oral
- Geriatric Formulations
- Homeopathic Formulations
- Hospice Consultation
  - Pain Formulations
  - Nausea Formulations
- Solutions
  - Inhalations & Other
- Suppositories
  - Rectal
  - Vaginal
- Suspensions
- Syrups
  - Pain Cocktails
  - Cough Syrups
- Trockes
  - Anti-Fungicidals
  - Anti-Smoking
  - Sublingual
  - Chewable
- Urethral Inserts
- Veterinary Formulations

We Carry Products from a Comprehensive Inventory of Suppliers:

Apotex
Ayurved Formulas
Biomed Products
Boiron Homeopathics
Country Life
Dolisos
En Garde
Enzymatic Research
Flora Complete
Gaia Herbs
Genestra
Holistic Int'l
Homeocan
Jamieson Products
Jarrow Formulas
Jason Winters
Karuna
Linus Pauling Products
Master Formulas
Natures Herbs
Nova
Homeopathics
Novopharm
Nutrition For Life
Nu Life
Phyto Pharmica
Purity Life
Quest
Seroyel
Swiss Herbal
Thorne Research
Thursday Plantation
Vital Treasures
Wampole "Kosher" Vitamins
White Hall Robbins
Zand Formulas

Complete Selection of Herbal Teas:

• Alvita • Bigelow • Celestial Seasonings • China Green • Flora • Kombucha • Select • Sir Jason Winters • Stash • Tatra • Traditionals • Yogi

Our Compounding and Integrative Pharmacists:

David Garshowitz, Boyana Djokic, Olga Karniol,
Mira Perovic, David Bergman,
Ildiko Illes, Al Kimson

In the Literature: The *UTMJ* Club

Andrew Lustig, BSc. (0T0), and
Sean Wharton, BScPhm, PharmD (0T1)

This section of the New and Views will present updates of recent advances in the medical and scientific literature. Critical appraisals of selected studies will highlight this section.

Tight Blood Pressure Control Reduces Death in Type II Diabetics (UKPDS –38 Trial)

Question: Can controlling blood pressure in diabetics prevent diabetic complication and death?

The United Kingdom Prospective Diabetes Study (UKPDS - 38) randomized 1148 patients with type II diabetes and hypertension into two groups. The first group maintained tight blood pressure control (BPC) (BP < 150/85), and the second group with less tight control (BP < 180/105). Patients were monitored for 8 years. Analysis was by intention to treat.

Note: Intention to treat (ITT) means that all patients were included in the statistical analysis, including the patients that dropped out of the study (for any reason). Dropouts are accounted for as failures. This favours a negative outcome for a study, thereby strengthening a positive result.

Patients allocated to tight BPC had reduced risk of developing any diabetes-related clinical end point (p = 0.005), diabetes-related death (p = 0.019), stroke (p = 0.013) and microvascular disease (p = 0.009), compared to the less tightly controlled patients. The relative risk reduction (RRR) for death was significant at 32.5%. (see Evidence Based Medicine article IV in this journal for an explanation of RRR) During the 8 years, the increased cost of therapy for the tight BPC group, compared to the less tight group was U.S. $1480/patient, but the reduced total cost of complications was $1898/patient, resulting in a net savings of $418/patient. This study may change the way clinicians treat type II diabetics, as these results indicate that tight blood BPC is better than less tight BPC and may even be more beneficial than tight blood glucose control.

Source: BMJ 1998;317:703-13.

Albumin May Increase Mortality

Question: Does human albumin reduce mortality in critically ill patients ?

The debate about whether to use colloids (e.g. Albumin) or crystalloids (e.g. NS, or D5W) for fluid resuscitation in seriously ill patients continues. A meta-analysis by the Cochrane Group reviewed 30 studies that compared albumin to no colloid or to a crystalloid in patients with hypovolemia due to surgery, trauma, burns or hypoalbuminemia. Albumin was associated with higher mortality for critically ill patients, patients with hypoalbuminemia, and patients with burns. Close inspection of the primary studies are needed in order to interpret this data about increased mortality, as there are other important influences on mortality in these patients that are not clearly reported. Clearly a large, well designed study is needed to further clarify this debate. The inability to apply the results of this study to patients demonstrates that meta-analysis studies are only as good as the primary literature selected.

Source: Cochrane Group. BMJ 1998;317:235-40.

Gingko Biloba Improves Dementia

Question: Is Gingko biloba effective at improving neurological function in Alzheimer's patients?

327 patients with Alzheimer's or multi-infarction dementia were enrolled in a randomized double-blind placebo-controlled trial to determine the effectiveness of gingko biloba (EGb 761). Gingko biloba is one of the most popular herbal medications in North America. It has a number of reported physiological effects including vasodilation, and effects on

neurotransmitters. Changes in eognitive impairment were assessed using the eognitive Alzheimer's Disease Assessment Seale (ADAS) and daily living and social behaviour seales. Intention to treat analysis was used. Follow up was for 52 weeks. The group of patients who reeeived placebo deterioрated more than the group who reeeived EGb 761. A elinieal improvement of > 4 points on the ADAS subseale was shown for 27% of patients treated with EGb eompared with 14% of patients treated with plaeebo. Experts reeommend that a trial with this drug may be worthwhile. EGb may have fewer side effeets than taerine, the only other pharmaeologieal treatment for Alzheimer's. Herbal medieation may be finding its way into the praetiee of Western medieine.

Source: Lebars PL et al. JAMA 1197;278:1327-32.

Chiropractic Manipulation and Physiotherapy Were Not Effective for Low Back Pain

Question: Is manipulation or physiotherapy effective for low back pain?

321 patients with low baek pain (LBP) were alloeated to physiotherapy by a MeKenzie Institute physiotherapist, ehiropraetie manipulation or to reeeive edueational booklets that ineluded adviee about promoting reeovery and preventing reeurrenee. At 4 weeks, the ehiropraetie group had less severe symptoms than the edueational group (p = 0.02). The groups did not differ for symptoms at 12 weeks, days of redueed aetivity, missed work, need for bed rest, or reeurrenee of LBP. The 2 year cumulative eost was U.S. $437, $429, $153 for the physieal therapy, ehiropraetie and edueation groups, respeetively. It should be noted that although this study does not support physieal therapy or ehiropraetie medieine as preferred primary intervention for LBP, neither approaeh seems to be harmful. These therapies may result in improved general satisfaetion in patients who aetively seek sueh eare. This study raises several questions. Should insurers pay for manual or physieal therapy for LBP, and is improved satisfaction worth the additional several hundred per patient? Are resourees better spent elsewhere, sueh as, for patients with spinal disease who would reeeive greater benefit? Eeonomie factors and patient demand will have to answers these questions.

Source: N Engl J Med 1998;339:1021-9.

ADHD Children Have Smaller Brain Volumes

According to a study presented during the Ameriean Aeademy of Neurology's 51st annual meeting in Toronto, children with attention defieit hyperactivity disorder (ADHD) have signifieantly smaller brain volumes than normal children. They also have several other struetural brain differences ineluding signifieantly less grey matter in their frontal brain region. The disorder, which often originates in ehildhood and is more eommon in boys than in girls, renders patients inattentive and hyperactive. As a result, affeeted ehildren may have trouble controlling their behaviour.

Source: AAN Conference 1999; Toronto, Ontario, Canada.

Confirmation that ICUs Staffed by Intensivist Saves Lives

A reeent artiele from Johns Hopkins published in the Journal of the Ameriean Medieal Assoeiation, indieates that some post surgieal patients are up to three times more likely to survive if their hospital's ICU is staffed by intensivists. The study also found that daily rounds by an ICU speeialist are "as important as the experienee of the surgeon." The study examined hospital diseharge data for 2,987 abdominal aortie aneurysm patients who were treated at 46 Maryland hospitals between 1994 and 1996, looking at mortality rates, hospital length of stay, and the number of days spent in the ICU.

Source. JAMA. 1999;281:1310-1317.

Aerosol Gene Therapy Effective in Cystic Fibrosis

A Mareh, 1999 study published in The Laneet found gene therapy to be effeetive in treating eystie fibrosis (CF). The study administered a normal version of the eystie fibrosis transmembrane conductanee regulator (CFTR) gene to CF patients in an aerosol. This resulted in a 25 pereent restoration of normal chloride transport function eompared to subjeets reeeiving plaeebo. Applying the teehniques used in this study to other diseases may hold the key to "euring" a myriad of genetie diseases.

Source: The Lancet 1999 353, 9157.

Another Good Reason to add Statins to the Tap Water (statins prevent deaths even if your cholesterol is normal)

A study presented at the Ameriean College of Cardiology eonferenee in New Orleans found that the HMG-CoA reduetase inhibitor simvastatin slows the progression of eoronary artery disease (CAD) in patients with normal levels of eholesterol and established CAD. This was the first time that the positive impact of lipid reduetion with simvastatin in CAD patients with normal cholesterol has been demonstrated. These results were from the SCAT (Simvastatin/Enalapril Coronary Atherosclerosis Trial), a double-blind randomized, plaeebo-eontrolled and multi-eentred study whieh involved 460 patients.

Source: ACC Conference 1999;New Orleans, Lousianna, USA.

UTMJ Series on Complementary and Alternative Medicine (CAM) Part 3:

Homeopathy: Has it Beaten Medicine at its Own Game?

Dan Perri, BScPhm (0T0)

"It is not as if our homeopathic brothers are asleep: far from it. They are awake to the importance of the scientific study of disease."

– Sir William Osler (1905)

The resurgence of homeopathy has been documented around the world and, in the Western World, may be due to perceived shortcomings of current medical management, fear of iatrogenic illness, and frustration with practitioners who can spare only a few minutes per patient. Perhaps this resurgence represents a greater acceptance of the claims of homeopathy by the public despite significant protest from the scientific community that it is impossible for homeopathy to offer anything more than a placebo effect. Whatever the reasons, "Western" physicians have cause for concern because a school of thought which they successfully managed to suppress in North America in the early 1900's has resurfaced in the form of a complimentary medicine industry whose ongoing annual growth far exceeds that of any other health industry. Furthermore, the discursive space (journals, symposia, etc.) which once maintained boundaries between "insiders" and "outsiders" has been penetrated by homeopathic proponents with some startling results. This paper does not aim to take a stand either for or against homeopathy but rather outlines recent trends in science and scientific philosophy, which demonstrate the need for physicians and medical trainees to take a more active role in learning about complimentary therapies.

History[1-3]

German physician Samuel Christian Friedrich Hahnemann (1755-1843), who had become dissatisfied with the standard practice of medicine, conceived homeopathy in the late 18th century. Homeopathy was to be a gentler medicine than the Heroic practices of bloodletting, purging, and blistering offered at that time. The word homeopathy was derived from the Greek words for like (homoios) and suffering (pathos). After ingesting some cinchona bark (from which quinine was derived) and having suffered from symptoms similar to malaria, Hahnemann developed homeopathy's first law, "similia similibus curentur," or let likes be cured by likes. In other words, drugs which cause specific symptoms in certain doses could, in different doses, be used to cure diseases which cause the same symptom complex. This became known as the Law of Similars. The other two major tenets of homeopathy include the Doctrine of Vital Force and the Doctrine of Minimal Dose. The Doctrine of Vital force asserts that disease is not due to any external agent but is merely a departure from health so that living organisms have a "vital energy" which can reject toxins based on spiritual changes in the body. The Doctrine of Minimal Dose states that potency of any cure increases with progressive dilution.

The most controversial principle of homeopathy is this use of minimal doses called the Law of Infinitesimal Doses. Homeopathic remedies are derived from plant, animal, and mineral substances macerated in 99 parts of hydroalcoholic solution (if soluble) or triturated in 99 parts of lactose and then diluted with more lactose until soluble in polar solvents. This original solution, known as the Mother Tincture, is then serially diluted and vigorously shaken (succussion) to increase its potency. It is believed that higher potency preparations (potentization) act longer, deal with "deeper" problems, and need fewer doses. Dilutions

may occur on a decimal scale (1:10) or Centesimal scale (1:100). Thus, a 1 in 10,000 dilution ratio would be 4X or 2C in the decimal and Centesimal scales, respectively. Low potency homeopathic products are generally less than 15C and high potencies are greater than 30C. Once the desired potency is obtained pellets of saccharose or lactose are impregnated with the solution or it is incorporated into alcoholic tinctures, cream bases, or syrups. The substance used to make the original solution is investigated by a process called "proving" in which healthy volunteers ingest the raw ingredient and record all of the physical, mental, and emotional changes they experience while taking the agent. Thus, when potentized, these agents would be used to treat conditions with similar symptom pictures.

Hahnemann considered disease in 3 major categories: sycosis, or fig-wort, which seems to equate with gonorrhea; syphilis; and psora (itch) which was an ill-defined, non-venereal "infectious" disorder that he believed was the underlying cause of 7/8ths of all problems including those that we would equate with illnesses including cancer, asthma, gout, and even mental disorders. Homeopathy differed in its treatment of disease from "mainstream" medicine because it treated psora-induced "imbalances" in the individual's physical, mental, and emotional states as a whole rather than correcting organ-system based pathology. This is referred to as the Principle of Individualization of therapy. These doctrines appeared unconnected to the medical community which had at about the same time embraced the logic and simplicity of Koch's Four Postulates of Disease. The great debate had begun.

At the heart of this debate is the fact that many homeopathic preparations dilute the "active ingredient" beyond Avogadro's number. Therefore, with dilutions greater than 6.02×10^{23} the laws of probability would predict that none of the molecules of the original substance would remain. This corresponds to a potency of 12C or 24X. Hahnemann and his followers believe that the vigorous shaking during the dilutions imparts a special energy to the solution which explains how dilutions beyond Avogadro's number are effective.

The Weakening Power of Scientism

From its inception, the idea of homeopathy caused great concern in academic circles primarily because of the "new" interest in science at the time. Homeopathy began in the era of "scientism" – a time in which there existed a belief that science was the ultimate authority to which all questions and problems can be directed and that scientists should be an intellectual elite, a ruling class of society. The reason that homeopathy remains controversial today may be, in fact, due to some undisclosed doctrine of scientism, in which reality and truth are thought to be singularly possessed by scientific inquiry with any deviation being clearly "irrational" rather than exemplifying a different rationality. The goal of modern science is "finalization" – the striving for the unification and completion of all knowledge. The idea in physics of "grand unifying schemes" typifies the search by scientists for general laws which are thought to be applicable in solving all problems.[4] Since homeopathy follows a clearly distinct paradigm from modern medicine, one which currently jeopardizes finalization, it is unlikely that the scientific community will imminently embrace it. Doing so may discredit what has become "science". Such was the case in what now is referred to as the "Benveniste Affair" in which "good science" capable of validating homeopathic doses caused biomedicine to resort to "bad science" to disprove it.

Dr. Jacques Benveniste is a respected French pharmacologist who while at INSERM (France's equivalent to the NIH) discovered that basophils reacted (released histamine from granules and changed their staining properties) when exposed to anti-IgE antibody dilutions up to 10 to the 120th power! He first submitted this research to *Nature* in August 1987. For obvious reasons, Nature believed that the research was flawed and, thinking that it would not be possible, required that the results be repeated in separate laboratories before publication. The study was replicated in four countries in several laboratories including University of Paris South, Hebrew University, University of Milano, and the University of Toronto. Finally, in June 1988, despite reservations, *Nature* published the results but not before including an editorial entitled "When to Believe the Unbelievable."[5] This editorial claims that the study "strikes at the roots of two centuries of observation and rationalization of physical phenomena," and summarizes that "what the article shows is that it is possible to dilute an aqueous solution of an antibody virtually indefinitely without the solution losing its biological activity." In the predictable fashion of orthodox medicine, *Nature* assembled a team to "investigate" the accuracy of the research at the University of Paris South. Their conclusion was that the research was not free from technical error or statistical inaccuracies. It should be mentioned that two of the three-man team were scientists unfamiliar with the immunologic methods used at INSERM 200 and that the third man was James "the Amazing" Randi – yes, the magician! Furthermore, this poorly assembled team spent only one week-end at the lab and conducted no investigation of labs in any of the other three countries. It is not surprising that Dr. Benveniste characterized the visit as "a mockery of scientific inquiry."

Can Modern Science Explain the Law of Potentization?

Benveniste was not alone in his discovery that therapeutic agents could work in low doses. In the 1870s research done by two independent researchers concluded that with certain pharmacologic agents, weak stimuli could accelerate physiologic action while strong stimuli could inhibit physiologic

action. This biphasic nature of a drug's action became known as the Arndt-Schulz law. This law can be used to explain the phenomena of increased bacterial growth with dilute iodine solutions but inhibition at high doses. Modern evidence of this was published in the journal *Haemostasis* in an article which showed that homeopathic doses of aspirin given to human subjects *shortened* bleeding time over placebo.[6] In homeopathic terms, then, aspirin could be potentized for use in the treatment of conditions of hypocoagulation. Similar studies have been performed using a variety of known toxins in homeopathic concentrations to stimulate growth and health in plants[7] and animal models.[8]

Reilly *et al.* demonstrated that the evidence for homeopathy is reproducible and greater than the placebo effect despite a lack of understanding of the mechanism of action.[9] Hahnemann felt that succussion imparted a special "energy" to the water or alcohol. In his work, Benveniste suggests that the original solution acts as a template which alters the electromagnetic properties of the water in which it is suspended.[5] The collaborators at the other labs also found that extreme antibody dilutions not vigorously shaken in a vortex had no pharmacologic effect whereas those that were shaken elicited a basophil response. Reilly suggested that "succussion produces energy storage in the bonds of the diluent in the infa-red spectrum which 'downloads' in contact with the water of living systems. Perhaps this information then spreads like a 'liquid crystal' through the body water, modifying receptor sites or enzyme action."[10] There does exist evidence that the NMR spectra of homeopathic-like dilutions are different than that of plain water subjected to the same succussion.[11] Recent studies have suggested that homeopathic medicines may work by promoting the formation of bizarre ice crystals which form at temperatures above freezing. These crystals, visible under electron microscopy, appear to give off a unique electrical field and so are called "IE" crystals – ice with an electric field. Benjamin Bonavida, an immunology professor at UCLA, found that IE water could stimulate the immune system with up to 100 times more biological activity than placebo.[12] Much of this work, however, is difficult to reproduce. Nonetheless, if there is any accuracy to it then it may someday explain both the Law of Similars and the Law of Infinitesimal Doses.

Evidence-Based Medicine: An Impetus for Homeopathy's Success?

Over the last dozen or so years the medical community has embraced an "evidence-based" approach which is rooted in double-blind, randomized, placebo-controlled trials. The goal of such trials is simple: study a possible therapeutic modality against a similar, yet inactive, agent. Randomized controlled trials (RCTs) are designed only to measure pharmacodynamic or physiologic outcomes, not to explain the mechanisms behind them. For this reason, any modality, including homeopathy can use RCTs to study the efficacy of various products despite limited knowledge of the mechanism of action of the tested agent. Both the academic and the general populations appear to have accepted RCTs as "good science." Reilly's findings in favour of homeopathy prompted him to ask "whether the reproducibility of evidence in favour of homeopathy is proof of its activity or proof of the clinical trial's capacity to produce false-positive results."[9]

A 1991 *British Medical Journal* meta-analysis on the clinical trials of homeopathy aimed to establish whether there was evidence of the efficacy of homeopathy from controlled human studies. The researchers assessed 107 trials in terms of methodology from a checklist of predefined criteria. The outcome of each trial was interpreted in relation to its quality. While most trials were of low quality, there was positive evidence in 81 trials. Regardless of their opinion about the quality of the trials, the researchers had no choice but to comment on the obviously positive trend in the results.[13] The major problem with the study is that it looked at the modality as a whole and not at specific diseases or homeopathic products. A 1997 meta-analysis in Lancet reviewed 185 trials of which 119 met the inclusion criteria but of which only 89 had adequate data for meta-analysis. The combined odds ratio for the 89 studies was 2.45 (95% CI 2.05, 2.93) in favour of homeopathy. Twenty-six of those studies were considered high quality and the odds ratio was 1.66 (1.33, 2.08) or 1.78 (1.03, 3.10) when corrected for publication bias. The interpretation of the data was that "the results of our meta-analysis are not compatible with the hypothesis that the clinical effects of homeopathy are completely due to placebo."[14] Once again it was suggested that there was little data looking at individualized homeopathy (i.e. patient-specific) or disease-specific data.

A meta-analysis on the use of homeopathy in postoperative ileus (6 of the 7 trials found were adequate for analysis) showed that overall there was a significantly reduced time to first flatus by 7.4 hours (95% CI 10.8 to 4 hours) in the homeopathy group.[15] A recent meta-analysis on RCTs of individualized homeopathy found 32 trials involving a total of 1778 patients. However, only 19 of these trials provided sufficient data for meta-analysis. The investigators found that individualized homeopathy was significantly more effective than placebo with a pooled rate ratio of 1.62 (95% CI 1.17 to 2.23).[16] It must be noted that all of these trials recommended further investigation since a significant number of trials had poor methodology. Nonetheless, the tool which biomedicine has developed as its "gold standard" for reporting efficacy appears to give homeopathy some credibility. While most of the data is derived from poor studies, the meta-analyses were of good quality, statistically-sound, and were published in leading peer-reviewed biomedical journals. For the general public, the statistics and study-design

are meaningless but the final interpretation of the data and the reputations of the journals are not.

Conclusion: Are Medicine and Homeopathy Really Different?

To the academic elite, homeopathy represents a scientific absurdity – a departure so far from current thought that, at best, it is considered a pseudoscience. Homeopaths argue that while biomedicine claims to follow a strict scientific method, it also routinely violates these norms. Physicians still prescribe medications whose exact mechanism of action is unknown. Medical decisions are sometimes made on epidemiologic data, which do not illustrate cause-and-effect. Randomized clinical trials of various agents may show no benefit despite well-documented pharmacologic activity or may show benefit despite the lack of a known pharmacologic effect. From this perspective, biomedicine too is a pseudoscience. When closely examining homeopathy and biomedicine one can see that they are both trying to appropriate scientific discourse in order to gain acceptance. They have complicated terminology, use scientific-seeming experiments to prove their validity, create academic institutions for their discipline, and employ technology for scientific-looking procedures.

The truth is that they are both adhering to principles of scientism in a society where fields of "marginal" status within a scientific framework can attract adherents simply by convincing the public that their basis is not merely mystical. Science can change. It was 200 years ago when medicine could only offer blood-letting, trephination, herbal cures, and leeches. It was only 100 years ago when modern medicine replaced homeopathy in North America. Today, leeches and herbs are back. This illustrates that old ideas never die. However, to some "scientists" the advancement of science may mean that they should. But, if society is prepared to allow itself to be slave to the concept of scientism then scientists (homeopaths and allopaths alike) should be working together, both with new ideas and old ones, in order to attain scientific finalism. Perhaps one day biomedicine will be able to explain homeopathy (or vice versa.) This does not at all seem far-fetched given the fact that it had taken scientists centuries to develop the technology needed to discover that the earth is round and then decades to convince the rest of the world that it was true. Now is the time that physicians should learn about homeopathy; not in order to accept it or practice it, but at the very least to offer more than "I don't know anything about that" as an answer to patients asking about homeopathy. Afterall, as Osler suggested in his reminder above, homeopaths have attempted to learn the basics of pharmacology just as they have learned human anatomy, physiology, and pathology. How scientific are we, the medical community, really being if we are not examining all of the data? As suggested by Bellavite and Signorini "the sum of the clinical observations and experimental findings is beginning to prove so extensive and intrinsically consistent that it is no longer possible to dodge the issue by acting as if this body of evidence simply did not exist."[1]

References

1. Bellavite P, Signorini A. (1995) *Homeopathy: A Frontier in Medical Science.* North Atlantic: Berkeley.
2. Nichols P. (1988) *Homeopathy and the Medical Profession.* Croom Helm: Beckenham, England.
3. Endler PC, Schulte J, eds. (1994) *Ultra High Dilution: Physiology and Physics.* Kluwer Academic: Dordrecht.
4. Redner, Harry. (1987) *The Ends of Science: an essay in scientific authority.* Westview Press: Boulder.
5. Davenas E, Beauvais F, Amara J, *et al.* (1988) "Human Basophil Degranulation Triggered by Very Dilute Antiserum Against IgE." *Nature.* 333: 816-18.
6. Doutremepuch O, de Seze D, Le Roy D. *et al.* (1990) "Aspirin at Very Low Dosage in Healthy Volunteers: Effects on Bleeding Time, Platelet Aggregation and Coagulation." *Haemostasis.* 20:99.
7. Boyd WE. (1942) "The Action of Microdoses of Mercuric Chloride on Diastase." *British Homeopathic Journal.* 32:106-11.
8. Linde K, Jonas WB, Melchart D, *et al.* (1994) "Critical Review and Meta-Analysis of Serial Agitated Dilutions in Experimental Toxicology." *Human and Experimental Toxicology.* 13: 481-92.
9. Reilly D, Taylor M, Beattie N, *et al.* (1994) "Is Evidence for Homeopathy Reproducible?" *Lancet.* 344: 1601-6.
10. Reilly D, Taylor M, McSharry C, *et al.* (1986) "Is Homeopathy a Placebo response? Controlled Trial of Homeopathic Potency with Pollen in Hayfever as Model." *Lancet.* ii: 881-6.
11. Demangeat JL, Demangeat C, Gries P, *et al.* (1992) "Modifications des temps de relaxation RMN a 4 MHz des Protons du Solvant dan les Tres Hautes Dilutions Salines de Silice/lactose." *J Med Nucl Biophy.* 16: 135-45.
12. Lo SY, Bonavida B, eds. (1997) *Proceedings of the First International Symposium on Physical, Chemical and Biological Properties of Stable Water (H2) Clusters.* World Scientific Publishing: Singapore.
13. Kleijnen P, Knipschild G, ter Riet G. (1991) "Clinical Trials of Homeopathy." *Brit Med J.* 302: 316-23.
14. Linde K, Clausis N, Ramirez G, *et al.* (1997) "Are the Clinical Effects of Homeopathy Placebo Effects? A Meta-analysis of Placebo-controlled trials." *Lancet.* 350(9081): 834-43.
15. Barnes J, Resch KL, Ernst E. (1997) "Homeopathy for Postoperative Ileus?" *J Clin Gastro.* 25: 628-33.
16. Linde K, Melchart D. (1998) "Randomized Controlled Trials of Individualized Homeopathy: a State-of-the-art Review." *J Altern Complement Med.* 4(4): 371-88.

The Cuerrier Decision: Public Health and the Criminalization of HIV Serostatus Non-Disclosure

Darrell Tan, BSc. (0T2)

At the end of September 1998, the Canadian Supreme Court ruled in the case *R. v Cuerrier* that Henry Cuerrier, an HIV-positive British Columbian man, was guilty of two cases of aggravated assault in having unprotected sex with two seronegative women.[1] Defining his actions as aggravated assault requires proof that a) his actions endangered the life of the complainants, and that b) the force must have been intentionally applied. Although both women consented to the sex with Cuerrier, the crown successfully argued that their consent to having sex was nullified because Cuerrier obtained it through fraud – in other words, because he did not disclose his serostatus to them.

This criminalization of non-disclosure may seem logical to many. But criminalization carries with it significant public health consequences: the risk of deterring individuals from seeking HIV testing by inducing fear of incarceration, an adverse effect on patient – provider relationships, a risk of lulling society into a false sense of protection by criminal law, and the infringement of civil liberties. This article will outline the events leading up to the court's decision, and will address the unfortunate consequences resulting from it.

The Case

The details of the case are as follows. Cuerrier first discovered he was HIV-positive in August 1992. Although a public health nurse told him that he should use condoms for sexual intercourse and that he should inform sexual partners of his status, he said he could not do so because of the small size of his community. Shortly thereafter he began a relationship with KM, involving frequent unprotected vaginal intercourse. She discussed sexually transmitted diseases with him within a week of first having sex, though HIV was not specifically mentioned. He told her that he had had recent sexual encounters with

Chesley Sheppard

women who themselves had had numerous sexual partners, and that he had tested HIV-negative several months earlier. Later in the relationship, after getting tested for HIV together, both partners were told of Cuerrier's HIV status. KM tested negative but was told she may require further tests. The couple continued having unprotected sex for 15 months thereafter.

Cuerrier began a sexual relationship with another woman, BH, several months later. She told him that she was concerned about diseases, without specifically mentioning HIV. Cuerrier again did not disclose his HIV status, and the couple used no condom for half of their 10 sexual encounters. After learning of his serostatus later on, BH confronted Cuerrier, who apologized and admitted he should have told her earlier.

The initial ruling acquitted Cuerrier on both counts, a decision that was upheld by the BC Court of Appeal. At the time of the initial hearing, both women tested HIV-negative. The Supreme Court overturned these two decisions, however, ruling that whenever non-disclosure when obtaining consent puts another individual at 'serious risk of bodily harm',[1a] the non-disclosure constitutes an act of fraud which vitiates consent. By nullifying both women's apparent consent, this interpretation renders Cuerrier's sexual relations with both partners cases of sexual assault.

Given this situation, few would dispute the claim that the women deserve justice for the risk of contracting HIV infection. Indeed, the goal of preventing HIV transmission has risen to the forefront of public attention over the past two decades, spurring changes in educational curricula, media advertisements and a wide range of other sectors of society. But the complexities of these two values - that of attaining justice and that of HIV prevention - make them interconnect in complex and significant ways. What should society do when these values come into conflict?

Deterring Voluntary Testing

The principal reason that some public health advocates are concerned about the Cuerrier decision is the very real prospect that criminalizing a failure to disclose one's HIV positive serostatus will deter people from being tested. This argument implies that someone at reasonable risk of being infected with the virus - and who should, therefore, seek an HIV antibody test in the interests of optimizing his or her health and of allowing preventative intervention - may no longer want to get the result at all. Discovering that one is HIV positive can be extremely stressful, given the prognosis, the distress of deciding who to tell, and other psychosocial issues. In the new context of criminalization, the prospect of incarceration will add just another factor into the process of deciding to be tested. In some cases, this obstacle may be enough to prevent people from seeking HIV testing altogether.

1a Significantly, the legal ambiguity of this stipulation is one of the factors leading the Cuerrier decision to have drawn considerable controversy from a legal perspective as well as a public health perspective.

Such deterrence from HIV testing would have significant negative impacts on public health. Voluntary HIV testing, along with supportive counselling and education programs, form the foundation of HIV prevention programs. In today's world, the news reports of miraculous successes with triple therapy, exciting new AIDS vaccine trials, and breakthroughs in medical research may erroneously allow people to view HIV with less urgency and hence to 'let down their guard'. Anything which erodes society's emphasis on the importance of HIV testing frustrates efforts to control the epidemic. This in turn limits opportunities for education, treatment, and support services that may have an effect in changing risk behaviour.

A further problem could be the potential of a negative impact on the nature of the patient - provider relationship. It is conceivable that doctors may be subpoenaed to appear in court to publicly testify about what they know about their patient's HIV serostatus, sexual practices and other information normally held in the strictest confidence. Under normal circumstances, any disclosure of confidential information, no matter how inconsequential it may seem, requires patient consent. This fundamental rule allows patients to develop stronger, trusting relationships with their care providers, which is a cornerstone of high quality health care. The only exception to this rule of maintaining patient confidentiality is that if a test result is positive, physicians are ethically obliged (though specific legal obligations vary between the provinces and territories) to notify sexual and drug-use partners that they may have been exposed to HIV.[2] Patients could, of course, avoid this reporting altogether by seeking anonymous or non-nominal HIV testing, which is offered by an increasing number of agencies in Canada. But the result remains that this risk of breached confidentiality, and more likely the fear of this risk, may become yet another barrier to HIV testing and to people with HIV / AIDS (PWAs) being able to disclose their status at all.

A False Sense of Security

During the course of the trial, numerous AIDS organizations, including the Canadian AIDS Society (CAS), the Canadian HIV / AIDS Legal Network (Network), and the BC Persons with AIDS Society (BCPWA) argued that public health endeavours are more effective than criminal sanctions in controlling AIDS. However, representing the majority decision, Justice Cory countered that "the criminal law does have a role to play both in deterring those infected with HIV from putting the lives of others at risk and in protecting the public from irresponsible individuals who refuse to comply with public health orders to restrain from high-risk activities . . . there is a real and urgent need to provide a measure of protection for those in the position of the complainants".[1]

Statements such as this within the Supreme Court's ruling have given AIDS activists a cause for concern. In a press release dated 3 September 1998, the same day the decision was handed down, both the CAS and the Network expressed their fear that criminalizing non-disclosure of HIV status will lull HIV-negative individuals into a false sense of security that the

Criminal Code, rather than safer sex, will protect them from HIV.[3] Arguing that the ruling may 'protect' society from HIV transmission undermines the fundamental public health message that the primary responsibility for preventing the spread of HIV rests on the partners themselves. Specifically, safer sex negotiations need to be based on an assumption of equality, in which both partners address issues of sexually transmitted infections and of using appropriate personal protection.

It is of interest, in this regard, that while both women in the Cuerrier case initiated discussions with Cuerrier about STDs, neither of the two women asked specifically about HIV. This fact alone by no means implicates them as 'guilty'; there is no way of assuring that Cuerrier in fact would have disclosed his serostatus under these circumstances. But this point emphasizes that there is still considerable 'space' for public health measures to assert themselves in the effort to contain HIV. Until Canadians are regularly inquiring about HIV status and other STDs when engaging in sexual relations, it is too early to rely on criminal law, which should only be used as a last resort.

Further, the number of people engaging in such alarming behaviour as Cuerrier is insignificant compared to the numbers of new HIV cases attributable to social vulnerability and inadequate prevention. In the words of Stephen Genden, President of New York City's Community Prescription Services and Vice-President of *POZ* magazine, "it would be one thing if we had perfect HIV prevention, and still there were people who were 'acting irresponsibly'. But we're not in that situation at all . . . I see the criminalization debate as a red herring - it diverts us from addressing the real problems with prevention and care. It allows us to feel like we're solving the crisis by going after these very specific and very weird situations when we're avoiding the much bigger problems that lead to most HIV transmissions".[4] Indeed, a primary flaw in the logic of incarceration is that it completely fails to promote behaviour change in both the person engaging in unacceptable behaviour and the population at large.

The Wrong Tool for the Right Cause?

Given the potential of the Cuerrier case ruling to undermine public health efforts by deterring people from voluntary testing, adversely affecting the patient-care provider relationship, and offering a false sense of 'protection', the frustration of AIDS organizations is understandable. To them, criminalization is the wrong tool for the common cause of reducing HIV transmissions in Canada. It is instructive, in this regard, to consider what some of the goals of criminalization are in the first place.

One such goal is to deter harmful behaviour. But is criminalization going to deter those who are willing to behave as Cuerrier did anyway? Historical efforts to prohibit drugs, alcohol, and various forms of sexual activity already demonstrate that human behaviour is often far too complex to be controlled through the distant, bureaucratic functions of the state judiciary.

Another goal is arguably to prevent harm to others through incarceration. But because unsafe sex and needle-sharing are common in prisons, where access to condoms, clean needles and needle-cleaning equipment is often scarce, this measure may in fact only serve to accelerate the spread of the epidemic.

Finally, a third goal of criminalization is to punish. But is this the right way to approach the challenge of AIDS? Doing so addresses only the small proportion of people who willfully infect others while exacerbating the stigmatization faced by other groups commonly, and possibly unfairly, associated with HIV - gay and bisexual men, sex trade workers, and injection drug users. In some cases, this effect of 'stigmatization' has already started, since many PWA organizations view decisions like *R. v. Cuerrier* in the same light as other North American laws and rulings aimed at people with HIV / AIDS. These include laws introducing mandatory 'names reporting' of HIV positive people, screening programs for pregnant women and prisoners, and in at least 29 states, the criminalization of knowingly exposing others to HIV.[5] Common to all these situations is an increasing demand for HIV-status disclosure - a trend which, some would argue, seriously curtails individual liberty. One of the seven Supreme Court Justices involved in the Cuerrier case, Justice MacLachlin, argued in her dissent that the definition of 'fraud' created by the majority restricts PWAs' civil liberties by essentially rendering disclosure of HIV positivity a prerequisite for consent to sexual intercourse.[2a] Elsewhere, it has been asserted that the internationally respected late AIDS activist and humanitarian Jonathan Mann would have been "appalled" at the decision to criminalize non-disclosure of HIV status; during Mann's career, "He made clear why confidentiality of HIV status was necessary for health and ethical reasons, and why laws that target people with HIV infection result in worse health for the individual targeted and for the community".[6] In this context, then, the notions of 'cracking down' on HIV and the 'fight against AIDS' start looking much more like a crackdown on PWAs.

For many, the goals of deterrence, harm prevention and punishment thus provide an inadequate justification for criminalization. According to an earlier ruling on the Cuerrier case by the BC Court of Appeal, "There is no recognized duty, enforceable through the criminal law power of the state, which requires a person to provide full disclosure of all known risks associated with sexual intercourse to his or her sexual partners as a condition precedent to the partner giving an effective consent to sexual intercourse. The criminal law of assault is, indeed, an unusual instrument for attempting to ensure safer sex".[7]

Public Health Alternatives

If safer sex is the goal, but judicial criminalization is an unsatisfactory means, what other alternatives might be of use?

2a The definition of fraud set out in the Criminal Code limits the types of fraud able to vitiate consent in sexual assault to cases which are dishonest about the 'nature and quality of the act'. The definition used in the Cuerrier decision expands the types of fraud able to vitiate consent to include cases where there is a) a dishonest representation, b) a risk of serious bodily harm, and c) evidence that consent was based upon this misrepresentation. MacLachlin's argument is that this effectively equates non-disclosure of the seropositive partner with an automatic lack of consent, thereby limiting the PWA's civil liberties.

Wayne Campbell, Chair of the BC Persons with AIDS Society states that "The vast majority of public health experts who are knowledgeable about AIDS agree that HIV transmission is best dealt with through a variety of public health initiatives - not through making HIV transmission a crime".[8] More specifically, AIDS organizations have advocated increased emphasis on public health laws, as outlined in an extensive policy document released in June 1997.[9] The report explains that public health laws, while differing somewhat between Canada's different jurisdictions, have three principal functions:

1. to classify transmissible diseases and specify what rules apply to each;
2. to impose obligations on infected persons to seek medical treatment, and obligations on others to report suspected cases of infection;
3. to bestow health authorities with powers for the protection of public health which at their most coercive can be quasi-criminal.

In the case of HIV transmission, health officials may require individuals to undergo medical examinations and treatment, and may order infected persons to conduct themselves so as to avoid transmitting the infection to others. In extreme cases, every province has the right to detain or 'incapacitate' people (in health-care settings such as hospitals) to prevent the spread of disease. Personalized counselling forms an integral part of all these measures.

The advantages such measures have over criminalization are numerous. Most importantly, since the ultimate goal of laws and rulings such as *R. v. Cuerrier* is to protect public health, the issue clearly falls under the express mandate of public health law rather than criminal law. By following this basic premise, society will avoid the negative consequences of criminalization discussed already. In addition, public health measures further the ultimate goal of health promotion by tailoring health interventions to fit an individual's specific circumstances and by keeping individuals in contact with health service providers. Criminalizing non-disclosure ignores the multiple factors which often make people unwilling or unable to disclose their HIV status. Such complex human behaviours are best addressed through personalized, supportive public health programs.

Finally, public health laws also carry the advantage of being less restrictive of individuals' civil liberties; public health orders (or at worst, detention in a hospital) are less restrictive than incarceration. In addition, public health policy proposed by the Ontario Advisory Committee on HIV/AIDS emphasize that interventions should "be the least invasive, least restrictive, reasonably available and likely to be effective" possible.[10] Similar policies have been adopted or proposed in Quebec, Manitoba and British Columbia.

Conclusion

Based on this discussion of the adverse public health implications of the Cuerrier decision, the major problems with the goals of criminalization, and the strengths of public health law alternatives, it is evident that while "criminal law is certainly better suited to punish and denounce . . . public health powers are preferable for achieving rehabilitation and incapacitation".[9] Returning to the specifics of the Cuerrier case, the only outstanding issue is how best to attain justice for the two women adversely affected by Cuerrier's behaviour. One avenue worth considering might be the opportunities provided through tort law[3a] or civil suits. Though not applicable in the Cuerrier case itself since neither of the women contracted HIV, civil suits would provide justice for the complainants while achieving many of the worthwhile goals of criminalization. Ultimately, however, perhaps the best institution for addressing this concern - and indeed for addressing the entire issue of criminalization to begin with - is Parliament.[4a] This idea is in fact mentioned in the Cuerrier ruling by dissenting Justice MacLachlin, who contends that by setting a new legal definition of fraud in this case, the court has overstepped its judicial boundaries.[1]

In closing, it should be noted that despite the daunting forecasts, the ultimate result of criminalization on public health outcomes remains to be seen. Because the ultimate goal of those arguing either side of this debate is to reduce the spread of HIV transmission, however, we must not allow the criminalization of non-disclosure of HIV status to divert attention away from initiatives which can make a true difference. Society must continue to work together to emphasize education about the syndrome and its modes of transmission, undertake efforts to address root causes of HIV vulnerability, and promote basic public health practices of voluntary testing, safer sex and shared responsibility for controlling the epidemic.

References

1. R. v. Cuerrier. [1998]. S.C.J. No. 64 (SCC)
2. Canadian Medical Association. (1995). *Counselling Guidelines for HIV Testing.* Canadian Medical Association: Ottawa.
3. http://222.aidslaw.ca/elements/cuerriersept03E.html
4. Hanssens, C. (1998). From Unsafe to Illegal. *POZ.* May 1998: 60-73.
5. Richardson, L. (1998). Wave of Laws Aimed at People With HIV. *New York Times.* 25 Sep 1998.
6. Schusky, RW. (1998). Jonathan Mann's Mantle. *Lancet.* 352 (9145): 2025.
7. *R. v. Cuerrier* (1996). 111 C.C.C. (3d) 261. (BC Court of Appeal).
8. (1998). *BCPWA News.* Sep-Oct 1998: 12.
9. Elliott, R. (1997).*Criminal Law and HIV/AIDS: Final Report.* Canadian HIV/AIDS Legal Network and the Canadian AIDS Society: Montréal.
10. Ontario Advisory Committee on HIV / AIDS. (1996). *Reducing HIV Transmission by People with HIV Who Are Unwilling or Unable to Take Appropriate Precautions.* Ontario Advisory Committee on HIV/AIDS: Toronto.
11. http://www.aidslaw.ca/elements/crimisumE.html.

3a Tort law might be better understood as 'personal injury law', in which a party which does injury to another is required to compensate the other party for its loss. It differs from criminal law in that its goal is to restore a state of 'equilibrium' between the parties involved and in that it is private in nature. Criminal law, in contrast, is public in nature, with the state or crown determining what forms of behaviour are unacceptable to society.

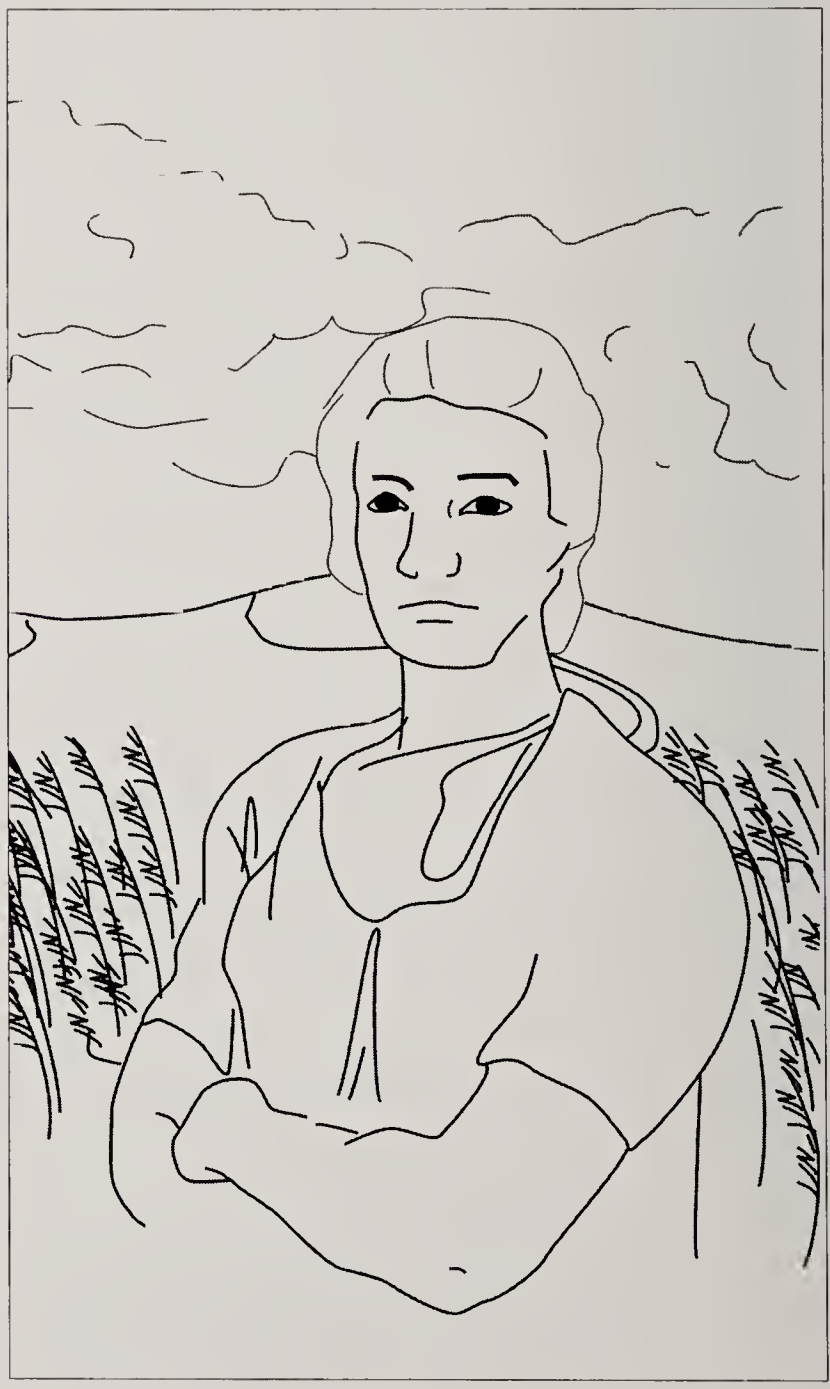
4a A bill (C-354) regarding HIV criminalization was in fact put before the House of Commons in October 1995, although the bill died only four months later.[11] The value of bringing the issue to Parliament would be that Canadian society would then have the opportunity to address the issue through existing democratic institutions, rather than by allowing the non-elected judiciary to decide this contentious issue on society's behalf.

Keeping Doctors North: Recruiting and Retaining Physicians in Underserviced Areas

Jason A. Shack, Bsc. (0T0), and Alison D. Baker, MSc. (0T1)

Abstract

The issue of recruitment and retention of rural physicians is a long-standing problem in Canada. Recent attempts at trying to solve the problem of underserviced areas have resulted in much hostility and little achievement. While the Canadian rural population has continued to grow, the number of physicians in these areas has steadily declined. This problem is not exclusive to Canada and work in other parts of the world, such as Australia, has been successful in increasing the numbers of rural physicians. An effective solution is complex and must encompass all aspects of a physician's training and career, including interventions prior to medical school, during medical school and postgraduate training, and continuing throughout medical practice. This paper outlines a comprehensive and integrated solution that is needed in order to solve Canada's problem of physician recruitment and retention in rural and underserviced areas.



Zacharo Roula Drossis

Introduction

Few would argue that Canada has a health care system with many enviable attributes, nor would many argue that this system has failed in a few key areas. One of these areas is the provision of medical care in rural and underserviced communities. Population need has continuously exceeded physician supply in rural and remote Canadian communities. While 23.5% of Canada's population lives in rural areas (communities of less than 10,000 people), only 17% of the country's family physicians and 3% of the specialists practice in these areas.[1] Within the last decade, the population of rural and small-town Ontario has increased by over 10%; in contrast, the number of physicians practicing in

these communities has decreased by 12% between 1994 and 1998.[2] In 1995, 63 designated underserviced communities in Ontario were trying to recruit 88 physicians; in 1997, the need increased to 68 communities seeking 116 physicians.[3] Provincial governments have tried to alleviate this discrepancy, but their 'solutions' have usually been met with hostility among medical students, residents, and practicing physicians. What follows is an outline of the problems that exist in providing health care in rural and underserviced areas and an integrated solution to the complex problem of recruiting and retaining rural physicians.

Defining the Problem

In 1995, Graham Scott, QC, a retired bureaucrat from the Ministry of Health published "The Scott Report."[4] This report was initiated on the observation that many small communities were unable to maintain adequate hospital-based emergency services. In a 1991 survey of Ontario small-hospital medical services, 44% reported a shortage of physicians willing to staff the emergency department and 71% predicted a shortage within 5 years.[5] The initial intent of the report was meant to focus on emergency care in rural areas; however, it uncovered many facts about rural practice as a whole.

The simplest and most easily overlooked finding of The Scott Report is that rural practice is different from urban or suburban practice. Rural doctors feel that others in the medical community do not recognize this difference and that rural medicine is not appreciated nor encouraged in most academic settings. The medical profession often views a rural physician as someone who is unable to succeed in larger centres such as Toronto. In reality, rural physicians perform three times as many procedures and work much harder for the same financial rewards as urban physicians.6 Many recent graduates are neither prepared nor oriented for rural practice, and family physicians coming out of a traditional residency often feel inadequately prepared for the specific demands of rural practice.

The added pressures and responsibilities of practicing in a rural area require a trade-off between income and lifestyle. Many young graduates are finding that working in an urban walk-in clinic can provide more satisfying earnings and a better lifestyle than can be achieved in a rural practice.[7] The small number of patients in rural areas often does not allow for high earnings, especially in the case of fee-for-service in low-volume rural emergency rooms. The frequency of unpaid on-call time, which may involve more than one night in five in a 24-hour emergency room, can cause problems with family and social life. A shortage of rural surgeons, as well as family physicians with additional training in anesthesia, emergency, obstetrics, and psychiatry, results in a more onerous on-call schedule for those with this training. For physicians who decide to settle in rural areas, a feeling of professional isolation, especially if in a solo practice, and a sense of abandonment by their medical associations, governments, and hospitals are major deterrents to their retention.[8]

The problem of physician recruitment and retention in rural areas is complex and requires examination of the three main areas of physician needs – professional satisfaction, financial remuneration, and lifestyle.[9] One reason that new graduates enter rural practice is the opportunity for a variety of medical experiences. This type of practice is limited in an urban centre with many specialists and frequent referrals. Also, most physicians in rural practice obtain a significant proportion of their incomes from hospital service. Cutbacks to the services provided by rural hospitals may result in physician attrition due to a lack of variety and challenges, as well as insufficient income.

Lifestyle issues as a whole are the major reason why physicians leave rural practice. A heavy workload resulting from too few doctors to share responsibilities often results in early physician burnout. In addition, the lack of anonymity in a small town may lead to physicians feeling that they have little personal time and no privacy. Single physicians may be faced with few social opportunities, and married physicians may have to deal with spousal discontent over lack of employment, along with the isolation. Only one of the factors of professional satisfaction, financial remuneration, or lifestyle has to be detrimentally affected to cause compromise of physician-based resources. Any solution to the problem of recruitment and retention of physicians in rural and underserviced areas must address all of these needs. A useful approach in defining the solution is to examine it at all levels of a rural physician's training and career.

Solving the Problem

The problem of recruiting and retaining rural physicians is complex and the interventions that have been implemented in Canada are proving to be only ineffective short-term measures. Australia has been a leader in rural health research and in solving the problem of their lack of rural physicians. They have had success with an integrated and multifaceted solution that starts early in the lives of potential rural physicians and follows through to supporting them in their rural practice.[10] Many Canadian medical groups understand that this type of approach is needed, as evidenced by a document recently released by the Ontario Regional Committee of the Society of Rural Physicians of Canada (SRPC) and the Professional Association of Internes and Residents of Ontario (PAIRO), which put the integrated solution into an Ontario context.[2]

Pre-Medical School Interventions

Individuals who come from a rural area are likely to return; thus, increasing the number of students in medical schools from rural areas would be a good place to start in address-

ing the problem of rural reeruitment.[11,12] One approach is to introduee rural physieians and medical students into rural high sehools to ereate an interest in rural medicine as a career and then support those students who express an interest. This type of program in Western Missouri has resulted in an inerease in rural applieants and entrants to an urban medieal sehool.[13] A program in Manitoba in whieh medieal students and rural family physieians visit high sehools has eaused an eight-fold inerease in the number of rural applieants to medical sehool.[14] Memorial University in Newfoundland provides opportunities for rural high sehool students to spend time at the medieal sehool during their regular breaks.[15] Promotion of medieine as a eareer ehoiee to rural high sehool students is something that is being done at the University of Toronto as part of the Outreaeh Program of the student-developed and student-led Rural Health Initiative. With support given to these types of programs, it is possible to inerease the number of rural students in medieal sehool; however, it is neeessary to provide a means of maintaining that interest throughout their edueation in an urban area.

Medical School Interventions

While eoming from a rural area inereases one's likelihood of returning to a rural area, not every rural doetor originally comes from a rural area. For this reason, programs at the level of the medieal sehool ean be used to maintain the interest of those from rural areas and also provide exposure for those who might never have eonsidered rural medicine.

Interest in, and enthusiasm for, rural medieine ean be sustained on-site at an urban medieal sehool by supporting the efforts of student rural health interest groups. These groups, sueh as those that have existed in Australia for years, and that are now appearing in Canada, have been shown to eneourage and maintain student interest in rural medieine.16 This type of foeus is needed to provide eollegial support for students interested in praeticing medicine in a vastly different way from that whieh is taught in the referral-based tertiary eare praetiee of most teaehing hospitals.

The key ehange needed in medieal school is to make time available early and throughout the eurrieulum for opportunities in rural medieine.[17] Like all things in medicine, the old adage "exposure, exposure, exposure" is also true for rural experienees. Medical students' partieipation in rural medieine has been shown to improve their pereeption of this speeialty and to inerease the likelihood of their ehoosing a rural eareer.[18] At present, this type of experienee is limited and diffieult to obtain. Medieal sehools need to faeilitate aeeess to rural eleetives, and resourees are needed for students to access rural preceptors. Financial resourees are also required to make these experienees viable. It is not helpful for medieal sehools to create a restricted database of rural physieians who are only able to aet as preeeptors for students from one school. Resourees are limited already and this type of approaeh will only worsen the problem. Medieal schools need to work together and support a single program to link interested medieal students with interested preceptors. An example of sueh a program has just been started by the Soeiety of Rural Physieians of Canada.[19]

Eaeh sehool, however, does need a eentral resource where students and faeulty ean access available rural medieine opportunities. This resouree ean be instituted by ereating a Rural Medieine Offiee at eaeh medieal sehool.[8] Ideally this offiee would arrange rural eleetives and provide aeeess to finaneial support, as well as providing a foeus for researeh in rural medieine. It would also play an advoeaey role in making necessary ehanges to the medieal eurrieulum to foster positive rural ideals and sensitize the entire faeulty to rural issues. In order to be meaningful, sueh an offiee needs to have eonneetions with, and partieipation of, rural physicians.

For students interested in praetieing urban medicine, finding mentors and role models in an urban medieal sehool is not diffieult; however, easy aeeess to sueh role models is lacking for students who have an interest in rural medieine. Changes in the organization of the university need to be made to inelude faeulty members who are not geographieally loeated on eampus.

Medieal schools should, of eourse, strive to ereate eompetent elinieians. They should also endeavor to train physieians who can funetion effeetively in a eommunity setting. In order to prepare students for eommunity praetiee, eommunity exposure is needed as part of medieal sehool training. Medieal sehools have to diversify and move into both urban and rural eommunities.[20] To some, this deeentralization is a very radieal and feared ehange; it is, however, similar to what has happened in the postgraduate training of family physieians in rural areas. In this way, medieal sehools will edueate eompetent physieians who are willing and prepared to praetice in rural and underservieed eommunities.

Postgraduate Program Interventions

Much like the undergraduate medieal currieulum, postgraduate training in tertiary and quaternary eare settings does not foster attitudes and praetiee patterns eondueive to rural praetiee. Those who train in a rural area, however, are more aeeustomed to praetieing in a rural area and more likely to stay praetieing there.[21] For this reason, postgraduate medieal training, as well as undergraduate training, should be deeentralized. To varying degrees, the opportunity to do some or all of their training in a rural area should be available to residents in every speeialty.

In regards to postgraduate training of family physicians, mueh positive ehange has been made. Programs sueh as the Family Medieine North program in Thunder Bay, Ontario

and the Northeastern Family Medicine Program in Sudbury, Ontario provide for an intense and independent environment to train rural family physicians in hope that they will stay and practice in these communities. Programs of this nature are not just limited to Ontario but are available to some degree in all Canadian provinces. It is appropriate that there be regional differences between the programs, but there should also be a core skill set that every rurally trained physician obtains. Standardizing a subset of skills necessary for licensure in rural practice could be accomplished by developing a national agreement outlining what these programs should offer.

Due to their limited population base, most rural areas are not conducive to a specialist's practice. The rural 'generalist' family physician must provide a wide variety of services, including those that are provided by specialists in larger urban areas. Presently, there are limited guidelines in place for the training, certification, and continuing medical education of rural family physicians with these advanced skill sets (e.g., anesthesia, obstetrics, and emergency medicine). Thus, there is a need for rural training programs that provide advanced skills training.[17] The ability to acquire, practice, and maintain a specialized skill set will require an integrated approach by the government, educational institutions, and the various licensing bodies. If this approach is taken, rural physicians can provide an increased number of services to their communities to avoid inconvenience of patient referral to a larger centre and relieve pressure on existing rural specialists.

Interventions for the Practicing Rural Physician

While the previously mentioned programs are very important to a comprehensive package in addressing the recruitment and retention of physicians to rural areas, probably the most important area of support and change is in regards to the practicing rural physician. Rural medicine is substantially different from that practiced by its urban and suburban counterparts. As a result, rural physicians need an organization that will give them a substantive voice to advocate for change and gain a feeling of empowerment over their professional lives.

Communities in underserviced areas can also implement changes to help address physician shortage and retention. The demographics and opportunities of a prospective community must first complement the practice and lifestyle interests of the physician to increase the chance of retention.[22] The funding of a community resource officer, whose job it is to recruit physicians to the area and match the interested physician with a suitable town, has been effective in Northwestern Ontario for a number of years.[23] A community resource officer has most recently been assigned to Northeastern Ontario, but there is still a need for officers in Southwestern, Southeastern, and Central Ontario.

The community itself can also become part of the solution. Underserviced areas can help by playing an active role in physician recruitment, providing a community-sponsored medical clinic, and supporting regional hospitals and their programs. The community should also assist in providing opportunities for the physician's spouse. Willing local governments could create a vibrant and dynamic environment to attract and enhance the lives of physicians and their families.

Every physician needs to maintain competence through continuing medical education (CME). CME is difficult to obtain in rural areas due to long travel distances, inability to obtain locum coverage, and a paucity of rurally relevant programs. The application of computers, the Internet, and the ability to teleconference will help solve the issue of distance for a subset of the CME that is required. These methods are not cheap, however, and financial support will be needed.[17] A novel and integrated solution to "hands-on" CME and locum coverage is found in a program provided by the Society of Rural Physicians of Canada. This CME program is provided by rural physicians for rural physicians, and the session facilitators both teach and provide locum coverage for those that participate.

The issue of financial support has always been contentious. Giving rural physicians more money is not a solution to the problem. The underserviced area financial incentives that have been tried have been reasonably good at recruitment but not at retention.[24] The traditional fee-for-service (FFS) payment scheme is not conducive to an effective rural practice.[6] Numerous plans have been initiated that all rely on some form of yearly salary based on services provided and special skill sets obtained. Given that each rural area is different though, no one plan is going to be a solution for all, and the government must have the courage to recognize this fact and allow for numerous flexible payment plans.

One of the most important issues that needs to be addressed when considering lifestyle is the frequency of on-call. It is generally accepted that call of more than 1 in 5 is not reasonable.[4,8] There are many communities, however, in which on-call of 1 in 2 is the average. While this type of schedule can be maintained for a short period of time, physicians become burned out and long-term relationships, both professional and personal, suffer. As well, the FFS method of payment is not an effective means of remuneration in rural areas where there is low volume of patients. An hourly rate for time on-call is one possible solution in attempting to make rural on-call compensation consistent

with that in urban areas. In addition, efforts to reduce call frequency, effective nurse triaging, and the possible use of nurse practitioners need to be explored.

Conclusion

The complexity of the problem of recruitment and retention of rural physicians requires a solution that is implemented at all stages of a rural physician's training and career. An integrated approach to problem solving requires not only interventions at the high school, university, medical school, and residency levels, but also the active participation and co-operation of the physicians, the communities in which they practice, and the regional and provincial governments.[8] If a coordinated effort is not taken, what will result is analogous to many horses trying to pull one cart in different directions. The outcome is much effort, but a broken cart. In Canada, this uncoordinated approach exists on the national, provincial, regional, and academic levels. The solution to addressing the needs of the increasing number of underserviced areas will be more effective and more expedient if a unified and national approach is taken to create comparable and effective programs and standardized curricula. Australia has successfully led the way in forming a national governing body on rural health and in the training of rural practitioners and can be an effective role model to Canada.[15] Graham Scott said it best: "it is time for everyone involved to show some courage and leadership and take some risks."[6]

Acknowledgment

Special thanks to Kim A. Ferguson, BSc. (OT1).

References

1. *SRPC.* (1998) http://www.srpc.ca/numbers.html.
2. *SRPC and PAIRO.* (1998) From education to sustainability: a blueprint for addressing physician recruitment and retention in rural and remote Ontario.
3. Sibbald B. (1998) Desperately seeking doctors. *CMAJ.* 158(3):377-8.
4. Scott, GWS. (1995) *Report of the fact finder on small/ rural hospital emergency department physician service.* Toronto: Ontario Ministry of Health.
5. Drummond A. (1998) A critique of the Scott Report. *Canadian Journal of Rural Medicine.* 3(1):27-30.
6. O'Reilly M. (1997) "Take some action, take some risk," conference on rural recruiting told. Canadian Medical Association Journal. 157(7):936-7.
7. SRPC. (1998) A doctor's review. http://www.srpc.ca/librarydocs/review.html.
8. SRPC. (1997) Recruitment and retention: consensus of the conference participants, Banff 1996. Canadian Journal of Rural Medicine. 2(1):28-31.
9. Irvine H, Rowntree C, and Thompson J. (1994) Needs of rural physicians. http://www.srpc.ca/needs.html.
10. Brooks J. (1994) Australia develops national strategy for bringing physicians to rural areas. *CMAJ.* 150(4):576-8.
11. Cullison S, Reid C and Colwill JM. (1976) Medical school admissions, specialty selection, and distribution of physicians. *JAMA.* 235:502-5.
12. Boulger JG. (1991) Family medicine education and rural health: a response to present and future needs. *Journal of Rural Health.* 7:105-15.
13. Calkins EV, Johnson A and Mares KR. (1978) Identification of rural-background applicants by the talent identification program of WMA-HEC. *J. Med. Ed.* 53:764-5.
14. Carter R. (1995) Training for rural practice: what's needed? *Canadian Family Physician.* 33:1713-5.
15. Rourke JTB. (1996) Education for rural practice in Canada and Australia. *Academic Medicine.* 70(5):464-9.
16. Kamien, M. (1995) Undergraduate rural incentives program: assisting medical schools to help solve the shortage of rural doctors. *The Medical Journal of Australia.* 162:228-9.
17. Wilson DR, Woodhead-Lyons SC and Moores DG. (1998) Alberta's Rural Physician Action Plan: an integrated approach to education, recruitment and retention. *CMAJ.* 158(3):351-5.
18. McAllister L, McEwen E, Williams V and Frost N. (1998) Rural attachments for students in the health professions: are they worthwhile? *Australian Journal of Rural Health.* 6(4):194-201.
19. http://www.srpc.ca/elective.html.
20. *WONCA Working Party on Training for Rural Practice.* (1995) WONCA policy on training for rural practice.
21. Magnus JH and Tollan A. (1993) Rural doctor recruitment: does medical education in rural districts recruit doctors to rural areas? *Medical Education.* 27:250-3.
22. Cullen TJ, Hart, LG, Whitcomb ME and Rosenblatt RA. (1997) The National Health Service Corps: rural physician service and retention. *Journal of the American Board of Family Practice.* 10(4):272-9.
23. *PAIRO.* (1996) Answering the call: towards an effective recruitment and retention program for communities and physicians in Ontario's underserviced areas.
24. Copeman WJ. (1987) The underserviced area program of the Ministry of Health of Ontario. *Canadian Family Physician.* 33:1683-5.

South-East Health Care Corporation / Soins de Santé du Sud-Est

Moncton Hospital

The Moncton Hospital is a 400 bed teaching hospital centrally located in the Maritimes. Referral population includes Eastern New Brunswick, Prince Edward Island and North-Western Nova Scotia. The city, with adjoining municipalities, has a population of more than 105,000 and was ranked as one of the 10 best Canadian cities for quality of community life. There is easy access to warm water beaches of the Northumberland Strait, and also the scenic Bay of Fundy area. Excellent availability of educational opportunities, cultural events and recreational activities in the immediate area.

We are currently recruiting family physicians and specialists.

Please reply to Dr. Donal Atkinson, VP, Patient Programs, 135 MacBeath Avenue, Moncton, NB, E1C 6Z8, telephone(506) 857-5532, fax (506) 857-5545, e-mail at doatkins@sehcc.health.nb.ca.

The Dwindles

Ra Han, BSc. (0T0), Mark Benaroia, BSc. (0T1), and
Barry J. Goldlist, MD, FRCPC, FACP*

The Scene

A conference room in a Toronto teaching hospital. Medical students, residents, and staff physicians are seated around a conference table. Jennifer, a third year medical student, David, a fourth year medical student, Karen, a PGY1 junior resident, and John, a PGY3 senior resident have encountered an interesting case on their team which Jennifer will present to the group. A faculty member, Dr. Smith, will facilitate a discussion of the case.

Jennifer: This is a 78-year-old widowed man with a history of type II diabetes mellitus and pacemaker who presented with generalized muscle weakness and "failure to thrive". He was seen at home by his family doctor who urgently referred him to hospital.

Dr. Smith: Let's pause here for a moment. Failure to thrive is a term generally used in the pediatric population. What does the term denote for the older patient, Karen?

Karen: Failure to thrive in the elderly is not a specific disease or diagnosis but a syndrome characterized by a gradual decline in physical and/or cognitive function, usually accompanied by poor appetite, weight loss, and social withdrawal.

Dr. Smith: That's right. David, most clinicians begin to formulate a differential diagnosis after hearing the chief complaint. What do you think the differential diagnosis of failure to thrive is?

David: Failure to thrive can be caused by a number of factors. Age-related physiologic changes, such as decreased muscle mass, impaired immune function, and decreased sympathetic response make the elderly more vulnerable to stressors. Any medical illness such as cancer; failure of organs such as heart, liver, or kidneys; chronic infection; endocrine diseases such as diabetes and hypo- or hyperthyroidism; and inflammatory processes such as temporal arteritis can cause failure to thrive.

Dr. Smith: Absolutely. The differential diagnosis of failure to thrive can encompass an entire textbook of internal medicine. The syndrome is usually multifactorial and so rather than finding a sole cause, we need to find all contributing conditions and treat those that we can. So we need more information before we can begin to sort this out. Jennifer, can you tell us more about the patient's history?

Jennifer: The patient's functional decline began 6 weeks ago. Previous to that, he had been doing well at home where he lived alone. He

* Chief, Conjoint Geriatric Program, Rehabilitation Institute of Toronto and The Toronto Hospital. Associate Professor, Department of Medicine, University of Toronto.

was able to ambulate around his house with a walker and received daily homemaking assistance. Then 6 weeks ago, he slid off a chair to the floor where he stayed for 16 hours before he was found. Since then, he has moved in with one of his daughters and is now unable to move in bed due to generalized weakness. His family helps him sit up in a chair during the day and is concerned because his appetite is poor and he has lost weight.

Dr. Smith: John, what does the tempo of this patient's decline in function suggest to you?

John: The temporal profile of the functional decline is important because it will give us clues as to what may be contributing to the patient's decline and whether or not it may be reversible. For example, an acute decline over days to weeks is an indication that there is most likely an underlying medical illness contributing to the patient's decline, rather than simply age-related changes, and that the patient has a higher chance of recovery once the medical illness is treated.

Dr. Smith: What are the details of the patient's past medical history?

Jennifer: The patient's past medical history includes a congenital right arm motor paralysis with decreased sensation; bradyarrhythmia managed with a pacemaker inserted in 1989; diverticulosis with hematochezia; type II diabetes mellitus controlled with oral hypoglycemic agents; peripheral vascular disease with a traumatic foot ulcer treated with oral antibiotics; and peripheral neuropathy with left leg weakness for the past 2 years.

Jennifer: Karen, what do you think of this list of medical problems?

Karen: Many elderly patients have multiple comorbidities that impact on their ability to maintain homeostasis. Hence, almost any medical illness can trigger a downward spiral of negative nitrogen balance, weight loss, decreased mobility, and undernutrition. For example, this patient has pre-existing neuropathies which limit his functional reserve to cope with additional stresses which affect his strength and mobility.

Dr. Smith: Polypharmacy is another common reason for failure to thrive. Have there been any recent change in the patient's medications?

Jennifer: The patient's medications are aspirin, metformin, glyburide, pentoxifylline, multivitamins, iron, and folic acid. None of these have been changed in the past 6 months. He had been taking ciprofloxacin and clindamycin for his foot ulcer but the course of antibiotics was completed on the day of admission.

Dr. Smith: Is there anything else on history?

Jennifer: The patient has a 50 pack year history of smoking but quit 20 years ago and he does not drink alcohol. A review of systems revealed a low grade fever a few weeks ago but none recently, bilateral leg edema, and incontinence secondary to immobility.

Dr. Smith: David, what do you think is the differential diagnosis for this patient's bilateral leg edema?

David: The differential diagnosis of edema includes congestive heart failure, nephrotic syndrome or renal failure, hepatic cirrhosis, and malnutrition. In heart failure, there may also be dyspnea, basilar crackles, an elevated JVP, and hepatomegaly with dependent, pitting edema. With nephrotic syndrome, renal failure, and malnutrition, the edema is generalized and often evident in the soft tissues of the face. With cirrhosis, there may be other signs of liver disease such as spider angiomas, jaundice, and collateral venous channels as well as ascites. Local inflammation, venous obstruction, and lymphatic obstruction can also cause edema but this edema is generally localized.

Dr. Smith: That's a very good approach to edema. With this patient, I would suspect a combination of malnutrition and dependency from spending most of his time in a chair. Jennifer, what did you find on the physical exam?

Jennifer: On examination, this thin, elderly man was in no apparent distress. His BP was 100/60, HR was 80 and regular, RR 20, and temp 36.7. His JVP was 2 cm above the sternal angle and he had no carotid bruits. On cardiac exam, he has a normal S1 and S2, no S3, no S4, with a grade 2/6 pansystolic murmur at the left lower sternal border with no radi-

ation. He has weak peripheral pulses palpable throughout. There was bilateral pitting edema to mid-thigh and a necrotie uleer on the dorsum of his left foot with no surrounding erythema or diseharge.

Dr. Smith: Let's stop there for a minute. Karen, what is the signifieanee of the patient's murmur?

Karen: A pansystolie murmur is suggestive of mitral or tricuspid valve regurgitation or a ventrieular septal defeet. Many elderly patients have murmurs due to ealeifieation of valves that are elinieally not important but beeause this murmur was not previously doeumented, it is diffieult to know what it signifies.

Dr. Smith: I agree. Continue with your findings, Jennifer.

Jennifer: On neurologieal exam, his fundi and eranial nerves were normal. He had a generalized deerease in musele bulk with no faseiculation and normal tone. His power was 3/5 in the left arm, 2/5 in the left leg, 0/5 in the right arm, and 4/5 in the right leg. He had absent deep tendon reflexes in his legs. On sensory exam, he had deereased vibration sense on his lower extremities to the knees but normal pain and temperature sensation. His gait and eoordination were diffieult to test due to his musele weakness. He seored 26/30 on the MMSE with 2 points off for orientation (wrong season, date off by one) and 2 points off on reeall (eould only reeall 1 of 3 words at 5 minutes). His MSK exam was normal and the remainder of his physieal exam was unremarkable.

Dr. Smith: David, what are the faetors other than eognitive impairment that influenee one's seore on the MMSE?

David: The MMSE seore ean be influeneed by the patient's flueney in English, hearing and visual impairment, patient cooperation, edueation level, patient's mental status, and how the examiner eonduets and seores the exam. If a patient is medieally ill, this ean have an effeet on the seore as well.

Dr. Smith: Jennifer, what did you find in your investigations?

Jennifer: The patient's bloodwork results are listed below. Of note, his previous hemoglobin 4 months ago was normal at 150.

Hb	115 (MCV 82)	Retic count	94
WBC	8.7	serum folate	32
Plt	240	B_{12}	390
ESR	62	Total Fe	4
		Ferritin	316
INR	1.11		
PTT	36		
Na	142	Cr	65
K	3.3	BUN	5.1
Cl	99	BS	8.4
HCO_3	27		
Ca	2.10	Protein	55
Mg	0.61	Albumin	32
AST	19	Amylase	139
ALT	8	T Bili	14
ALP	77		

Beeause we were eoneerned about his murmur, espeeially with a paeemaker, we requested an ECG and eehoeardiogram. We also have also requested a neurology eonsult regarding his musele weakness and peripheral neuropathy. The physiotherapist, oeeupational therapist, and dietieian were also eonsulted.

Dr. Smith: That eertainly sounds like a good start. It is important to get multiple speeialties and disciplines involved in taekling sueh a eomplex presentation. What happened in hospital?

Jennifer: Two days after he was admitted, the patient developed a fever of 38°C with ehills and diaphoresis. Blood eultures done at that time showed Gram positive eoeei in elusters in both bottles. The urine culture and a eulture of his foot uleer were negative. The echoeardiogram was also done that day whieh showed severe trieuspid regurgitation with a large vegetation on the anterior trieuspid valve leaflet. A seeond vegetation was also seen attaehed to the right atrial paeer wire.

Dr. Smith: David, what is the diagnosis?

David: The patient fulfils both of the major eriteria for infeetive endoearditis and henee meets the clinieal diagnosis for definite infeetive endoearditis.

Dr. Smith: Karen, why do you think that it was difficult to arrive at the diagnosis of infective endocarditis at the time of admission?

Karen: Our patient had a number of comorbidities which provided explanations for his clinical presentation. His prior low grade fever could have been explained by his infected foot ulcer. Then, because he was on antibiotics for his foot ulcer, he did not have a fever on presentation despite infective endocarditis. He also had hematochezia due to diverticulosis which might have explained his anemia. Other findings, such as the murmur and elevated ESR, were nonspecific. Also, our patient did not develop petechiae, splinter hemorrhages, Roth's spots, Osler's nodes, and Janeway lesions which are more specific to infective endocarditis but are not commonly found. Finally, our patient had an atypical presentation in that most patients with infective endocarditis would not present with such severe functional decline and muscle weakness.

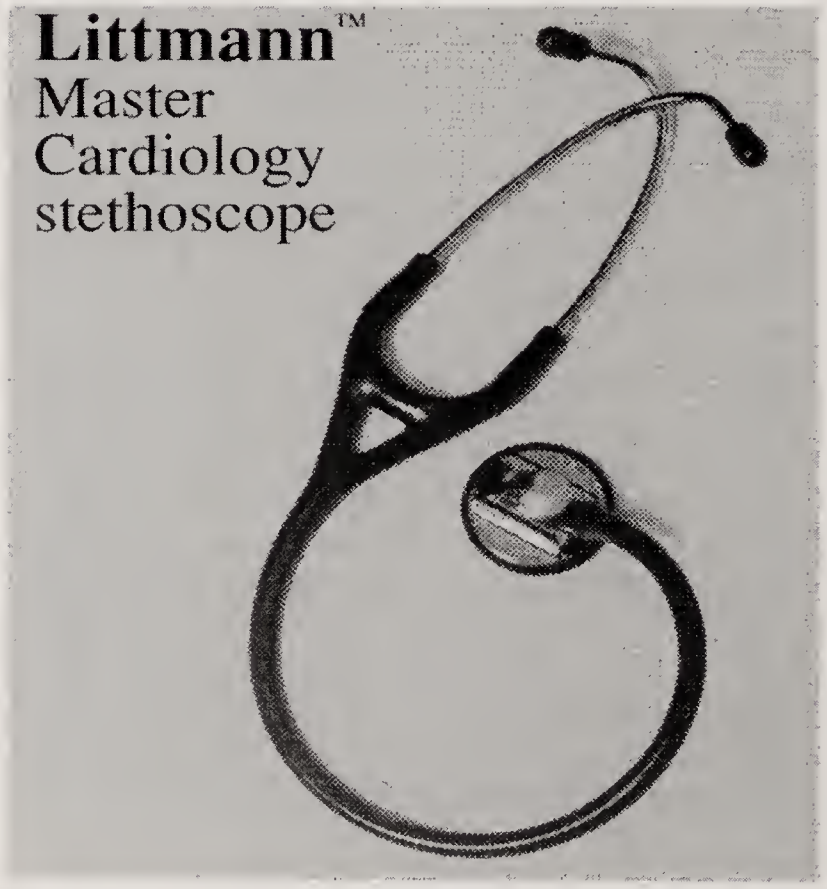
Dr. Smith: It was certainly a complicated picture. How did you treat the patient, Jennifer?

Jennifer: Cardiac surgery was consulted and felt that removing the infected pacemaker wire would be too high risk. Hence, the patient was started on vancomycin, gentamycin, and rifampin in consultation with infectious diseases. The patient will stop the vancomycin after 6 weeks but will continue with the gentamycin and rifampin for life. A repeat echocardiogram showed a decrease in the size of the vegetations. The patient also received physiotherapy and occupational therapy while in hospital and his level of functioning gradually improved. He was able to be discharged home to live with his daughter and will receive home care assistance.

Dr. Smith: Thank you for presenting this interesting case.

Clinical Pearls

1. Patients with failure to thrive can present with very nonspecific signs and symptoms. A comprehensive history and physical exam are important in directing appropriate investigations.
2. In failure to thrive, a tempo of decline over days to weeks indicates that the cause is more likely to be an underlying medical illness which may be reversible.
3. Due to the decrease in functional reserve with aging, almost anything can impair function. Hence, all potential contributing factors must be identified and treated if possible.
4. Most clinical and laboratory findings in infective endocarditis are nonsensitive and nonspecific. In patients currently or recently treated with antibiotics, lack of fever and negative blood cultures do not rule out infective endocarditis.



Acoustical excellence,
innovative design,
unmatched performance
3M

References

1. Egbert AM. (1993). 'The dwindles', failure to thrive in older patients. *Postgraduate Medicine* 94:199-212.
2. Palmer RM. (1990). 'Failure to thrive' in the elderly: diagnosis and management. *Geriatrics* 45:47-55.
3. Roubenoff R and Harris TB. (1997). Failure to thrive, sarcopenia, and functional decline in the elderly. *Clinics in Geriatric Medicine* 13:613-622.
4. Verdery, RB. (1997). Clinical evaluation of failure to thrive in older people. *Clinics in Geriatric Medicine* 13:769-778.
5. Verdery, RB. (1995). Failure to thrive in the elderly. *Clinics in Geriatric Medicine* 11:653-659.

A Case of Confusion

Joanna Holland

Presenation of Case

A 78 year old right-handed man with a two year history of gradual cognitive decline was admitted to the hospital with increased confusion following three days of hallucinations and several episodes of midsternal chest pain.

The patient was well until two years prior to admission when his wife noticed that he was becoming slower at many of his normal activities. He became increasingly dependent on her for many functions that he used to handle easily, including his finances. It took him longer and longer to balance his bankbooks, and his son began doing his income taxes. He became increasingly anxious and indecisive and experienced episodes of nighttime confusion and disorientation. He was found wandering, unable to recall where he was going. He asked "When are we going home?" when he was in fact at home. He developed dressing dyspraxia and required assistance from his wife to dress. Several months before admission, his wife noted that a tremor had developed. Sertraline and diazepam were administered, but with little improvement, and these were discontinued.

Two weeks prior to admission he was seen by a psychiatrist because of increasing anxiety and sleep disturbance. He was well dressed and groomed, but appeared anxious and hesitant, turning frequently to his wife for direction and support. He was unable to clearly state a chief complaint and denied any specific preoccupations or worries. He denied any problems with appetite or sleep, however his wife insisted that sleep disturbance was a major concern.

The patient was a retired accountant who lived with his wife in their own home. They had eight children. He had previously smoked about five cigarettes per day; but had stopped fifteen years ago. He was taking no medications. Past medical history was non-contributory and there was no family history of dementia or psychiatric disorder.

On examination he was relaxed, discursive and smiling responsively, but with some evidence of psychomotor retardation. He had both a mild resting tremor and intention tremor, bilateral cogwheeling and a masked facies. He did not extinguish on glabellar tap. Formal cognitive testing revealed significant word-finding difficulties, impairment in general knowledge, and difficulty with semantic priming and word generation. Abstract thinking was impaired and he showed extinction on bilateral stimulation and significant visuospatial deficits on clock-drawing. His mini-mental status score was 24/30. The psychiatrist's impression was that the patient was not suffering from a primary psychiatric disorder.

Over the next two weeks, his decline accelerated. He began to have visual and auditory hallucinations and paranoia; he believed other people were in the room with him. He was frequently hyperactive and agitated. He had one serious fall in which he injured his arm.

He presented to the hospital with a complaint of several 30 minute episodes of chest pain. On admission to the hospital, he did not look unwell. He was confused as to the date. He was initially restless, combative and violent, and haloperidol and midazolam were administered. He reported that his chest pain had not recurred. It had been mid-sternal and did not radiate. There was no dyspnea, no diaphoresis, and no history of congestive heart failure, exertional anxiety or recent ankle edema. The blood pressure was 160/100 mmHg but the general physical examination was otherwise normal. A chest radiograph and EKG were normal. Routine laboratory tests and levels of vit-

amin B12 and folic acid showed a CK elevation of 995 with a negative MB fraction. Laboratory values are shown in tables 1 and 2. Urinalysis was normal. He was given ASA and lorazepam.

Table 1
Blood Chemical Values on Admission to Hospital

Variable	Value	Normal Range
Sodium (mmol/L)	138	135-147
Potassium (mmol/L)	3.5	3.5-5.0
Chloride (mmol/L)	100	96-108
Carbon dioxide (mmol/L)	28	22-30
Urea (mmol/L)	4.6	3.0-7.0
Creatinine (mmol/L)	110	70-165
Glucose (mmol/L)	5.3	4.0-8.0
Calcium (mmol/L)	2.06	2.20-2.60
Phosphate (mmol/L)	0.8	0.8-1.5
Magnesium (mmol/L)	1.0	0.7-1.1
Total Bilirubin (mmol/L)	15	2-20
albumin (g/L)	35	35-50
ALT (U/L)	29	<40
ALP (U/L)	79	40-120
AST (U/L)	59	<37
Creatine Phosphokinase (U/L)	776	10-70
MB mass	11	<5% CK

Table 2
Hematologic Laboratory Values

Variable	Value	Normal Range
Hemoglobin (gm/L)	135	135-170
Hematocrit (L/L)	0.41	0.400-0.500
Mean Corpuscular Volume (fL)	87.8	80-100
Platelet count (109/L)	193	150-400
White-cell count (109/L)	6.2	4.0-11.0
INR	1.14	0.81-1.20
TSH (mIU/L)	4.0	0.5-5.5
Vitamin B12 (pmol/L)	210	140-750
RBC folate (nmol/L)	941	255-1000

A non contrast CT scan of the head was done and showed some atrophy but no bleeding or mass and was otherwise normal.

In the hospital, his cognitive dysfunction became more overt, with obvious disorientation, visual and auditory hallucination, mood swings and occasional episodes of aggressive behaviour. No metabolic cause for cognitive impairment was determined. Blood and urine cultures and syphilis serology were negative. On the third hospital day a neurological examination was performed. The patient was immobile, with masked facies and infrequent blinking. His speech was muttered and indistinct, and he exhibited a pill-rolling tremor in both hands and wrists, somewhat more marked on the left. He was completely disoriented in time and space, describing his whereabouts as "a self-serve hotel". He could give no useful account of what was wrong or how he came to be in the hospital. Registration was poor and he required several attempts to repeat three objects. Recall was worse; he could repeat only one of the three objects at two minutes. He could not spell world backward nor subtract serial sevens with any accuracy. He had trouble naming a watch held in front of him, but it was not clear that he understood the command. The snout and jawjerk reflexes were present. He had clear rigidity in upper and lower limbs. Stretch reflexes were not hyperactive and toes were downgoing. Horizontal gaze was full without nystagmus, but there were significant limitations of upgaze and downgaze.

On the seventh hospital day, the patient developed respiratory distress, and a chest radiograph showed increased density in the left retrocardiac region with small bilateral pleural effusions, most likely representing pneumonia. The family requested palliative measures only, and the patient died on the tenth hospital day.

Differential Diagnosis

Dementia is a clinical syndrome characterized by a deterioration of memory and other cognitive abilities such as language, visuospatial ability and praxis. The deterioration is not due to delirium or acute illness, and it impairs the previously successful performance of activities of daily living. These cognitive changes may coexist with various degrees of change in personality and behaviour.[1]

To summarize this case, this 76 year old man had a two year history of progressive and accelerating cognitive decline. His illness was initially characterized by confusion and disorientation, language deficits, dyspraxia and dyscalculia. He also experienced anxiety. Later, motor deficits consistent with the presence of mild parkinsonism developed. Clinical testing showed cogwheel rigidity, tremor, and a mask-like facies. Visual and auditory hallucinations, hyperactivity and agitation then developed, and the patient had episodes of aggressive and had one serious fall.

What can explain these clinical findings? Distinguishing among the numerous causes of dementia can be a difficult task. Major categories of causes of dementia include degenerative, vascular, metabolic, infectious and structural causes (Table 3). The clinical history and physical examination remain the cornerstone of the differential diagnosis of dementia, with assistance from laboratory tests and imaging studies. The history should focus on the onset, duration and tempo of the cognitive impairment. Noncognitive symptoms such as depression, delusions and hallucinations should also be specifically elicited. The physical examination should look for other signs of nervous system involvement, and other systemic disease. Cognitive assessment with the mini-mental status examination cannot distinguish between causes of dementia, but can be used to provide a rough estimate of severity and follow the progression of the illness.[2]

Table 3
Some Major Causes of Dementia

Degenerative
- · Alzheimer's disease
- · Diffuse Lewy body disease
- · Parkinson's Disease
- · Pick's Disease
- · Huntington's Disease
- · Progressive supranuclear palsy

Vascular
- · Multi-infarct
- · Diffuse white matter disease (Binswanger's)

Metabolic
- · Endocrine and other organ failure
  - -hypothyroidism*
  - - hypoglycemia*
  - - adrenal insufficiency and Cushing's syndrome*
  - - hypo- and hyperparathyroidism*
  - - renal failure*
  - - liver failure*
- · Toxic disorders
  - - Alcoholism*
  - - Drug, medication and narcotic poisoning*
  - - heavy metal intoxication*

Infectious
- · HIV
- · Neurosyphilis*
- · Prion (Creutzfeldt-Jakob disease)

Structural
- · Dementia pugilistica (boxer's encephalopathy)
- · Cerebral tumour*
- · Chronic subdural hematoma*
- · Normal pressure hydrocephalus*

**Indicates potentially treatable dementias (From Reference 4)*

Although they are rare, comprising only about 5% of all dementias,[2] any potentially correctable causes of dementia should be identified. These include many of the metabolic, infectious and structural causes of dementia. Some may have distinctive clinical signs, and laboratory tests are helpful. Even when a cause has been determined, it is useful to search for contributing factors. Blood tests recommended as routine include complete blood count, serum electrolytes including calcium, glucose, BUN, creatinine, liver enzymes, thyroid function tests, vitamin B12 levels and serologic tests for syphilis.[2] In the proper clinical context, other tests may be useful, such as a lumbar puncture for the diagnosis of the chronic meningitides or metastatic carcinoma, EEG when Creutzfeldt-Jakob disease is under consideration, or HIV or Lyme titres. It is also important to identify and treat depression, as depressive syndromes in the elderly can present with cognitive impairment, particularly affecting memory and concentration.[3] The possibility of drug toxicity requires a special consideration in older patients, who often take several medications and may be particular sensitive to side-effects.[2] In this patient, the common metabolic and infectious diseases that cause dementia have been ruled out by the laboratory findings, and there is no sign of any systemic disease. In the past he has not responded to anti-depressants, and at the time of admission he was not taking any medications. Toxic and Metabolic disturbances, and depressive disorder are therefore unlikely.

Neuroimaging studies, especially non-contrast CT scans, are often used in the diagnosis of dementia. They can reveal atrophy, white matter changes, vascular disease, and space occupying lesions such as meningioma and chronic subdural hematoma. A non-contrast CT scan in this case revealed non-specific cerebral cortical atrophy and was otherwise normal, ruling out the above causes for the dementia. The observation of atrophy is not generally helpful in the diagnosis of dementia, as it may occur as part of the normal aging process.[2]

The timing and mode of onset of deterioration are critical in determining the cause of dementia. Multi-infarct dementia, for example, is characterized by a sudden onset of disease and stepwise decline in cognitive function, rather than the gradual onset and progressive course seen here. It is also usually associated with focal neurological signs such as asymmetric reflexes, and there is often evidence of vascular insufficiency elsewhere, including ischemic heart disease and peripheral vascular disease.[2]

The two year history of gradual decline suggests a degenerative cause for this patient's dementia. It can be difficult to distinguish between the degenerative dementias. Although there are interesting findings regarding potential biologic markers such as blood analyses for the e4 allele of apoliprotein E, and volumetric MRI studies to detect atrophy in specific areas of the brain, these are still in a development phase. Neuropathological examination is usually considered the gold standard for the diagnosis of degenerative dementias, but the clinical history and findings on physical examination provide the most valuable diagnostic information during life.

The most common form of degenerative dementia is Alzheimer's disease.[1] It is typically characterized by memory loss, language impairment and visuospatial disturbances. Patients may also appear indifferent and suffer from delusions and agitation, particularly in the later stages of the disease. While these features occur in this patient, other important features distinguish his disease from Alzheimer's disease, in particular the extrapyramidal and neuropsychiatric features. The patient exhibited extrapyramidal signs early in his disease, including a resting and intention tremor, bilateral cogwheeling and a masked facies. In hospital his condition worsened and he became immobile and developed limitations of vertical eye movement. Late in the course of his illness he also developed the neuropsychiatric symptoms of visual and auditory hallucinations and paranoia.

The most common conditions in which dementia and extrapyramidal signs may coexist are Alzheimer's disease, idio-

pathic Parkinson's disease, and diffuse Lewy body disease. While extrapyramidal signs are common in Alzheimer's Disease, occurring in up to 30% of patients, they generally occur at a late stage, when patients are severely impaired.[1] In contrast, in this case these symptoms occurred when the cognitive deficits were mild to moderate. Dementia may also develop in idiopathic Parkinson's Disease. However this is an unlikely diagnosis in this case because the dementia preceded the parkinsonism.

Less common causes of parkinsonism with dementia and neuropsychiatric disturbances may also be considered (Table 4). Progressive supranuclear palsy is the next most commonly encountered disorder.[1] Usually it begins with a downward gaze impairment and progresses slowly to include rigidity and sometimes dementia. Slowing of motor processes, memory and visuospatial disturbances, clumsiness, dysarthria, postural instability and gait disturbance are common, and photophobia and seizures may also occur. The eye movement abnormalities occasionally do not occur for months or even a year or two after the other symptoms, and therefore an unusual presentation of this cannot be ruled out.

Normal pressure hydrocephalus usually presents with an ataxic or apractic gait and urinary incontinence early in the course of dementia.[4] Neuroimaging studies of the brain reveal enlarged lateral ventricles with little or no cortical atrophy. Binswanger's disease causes a patchy loss of white matter with a spectrum of presentations.[4] It may be associated with rigidity and other extrapyramidal signs but MRI scans typically show extensive signal abnormalities in the white matter, so it is unlikely in this case. Pick's disease is a frontotemporal dementia in which patients exhibit socially inappropriate behaviour, disinhibition and impaired judgement, but with relatively preserved constructional, calculating and memory function.[1] The deficits in judgement or social comportment are generally out of proportion to the memory deficits. A diagnosis of Creutzfeldt-Jakob disease is possible in the case of a patient with cognitive impairment and extrapyramidal signs.[1] One variant of this disease is typically associated with florid visual hallucinations, but they are accompanied by the development of cortical blindness, which was not evident in this case. Seizures are also common. Furthermore, the clinical course of CJD is usually more rapid, occurring over weeks to months. Huntington's disease as a first-time diagnosis is not usually a consideration in the elderly.[2] None of these disorders appear to be compatible with the findings in the patient under discussion.

The clinical characteristics of this case are most suggestive of diffuse Lewy body disease. Diffuse Lewy body disease, like Alzheimer's disease, is definitively diagnosed neuropathologically. Its pathological diagnosis is based on the presence of Lewy bodies, which are neuronal intracytoplasmic inclusions, in a widespread distribution throughout the brain, including the cerebral cortex.[5,6] Lewy bodies were originally identified as the hallmark of idiopathic Parkinson's disease, where they are found in selected brain-stem nuclei but not in the cortex. Their presence in the brains of patients with dementia was previously considered mainly as a neuropathologic entity without clinical correlation, or a variant of Alzheimer's disease, and it has only recently been recognized that it presents with a characteristic clinical syndrome (Table 5). Diffuse Lewy body disease may be the second most common cause of dementia following Alzheimer's disease. Its terminology and classification has been confusing, as numerous terms have been used to describe the disease, including Lewy body dementia and diffuse cortical Lewy body disease.[6]

Table 4
Major Causes of Dementia with Extrapyramidal Signs

Idiopathic Parkinson's Disease
Alzheimer's Disease-late stage
Diffuse Lewy Body Disease
Multi-infarct state
Binswanger's disease
Normal Pressure hydrocephalus
Pick's disease
Progressive supranuclear palsy
Cortical-basal ganglionic degeneration
Huntington's disease
Parkinson-dementia-amyotrophic lateral sclerosis complex of Guam
Dementia puglilistica
Wilson's disease
Manganese toxicity

From Reference 6

Table 5
Consensus criteria for the clinical diagnosis of probable and possible Diffuse Lewy Body disease

1 The central feature required for a diagnosis of DLBD is progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention and of frontal-subcortical skills and visuospatial ability may be especially prominent.

2. Two of the following core features are essential for a diagnosis of probable DLB, and one is essential for possible DLB:
a Fluctuating cognition with pronounced variations in attention and alertness
b Recurrent visual hallucinations that are typically well formed and detailed
c Spontaneous motor features of parkinsonism

1 Features supportive of the diagnosis are
a Repeated falls
b Syncope
c Transient loss of consciousness
d Neuroleptic sensitivity
e Systematized delusions
f Hallucinations in other modalities

1 A diagnosis of DLB is less likely in the presence of
a Stroke disease, evident as focal neurologic signs or on brain imaging
b Evidence on physical examination and investigation of any physical illness or other brain disorder sufficient to account for the clinical picture.

From Reference 5

Some features of diffuse Lewy body disease are similar to those of Alzheimer's disease, including deficits in attention, frontal-subcortical functions, and visuospatial abilities. As in Alzheimer's disease, the impairment of short term memory is greater than that of long term memory. The major features of dementia with Lewy bodies that distinguish it from Alzheimer's disease include fluctuating cognitive impairment with episodic delirium, prominent psychiatric symptoms including mood changes and visual hallucinations, and extrapyramidal symptoms occurring spontaneously or in response to neuroleptic medications.[5,6] Patients with this form of dementia are extremely susceptible to neuroleptic-induced parkinsonism, even with agents that do not commonly induce parkinsonism. The parkinsonism of dementia with Lewy bodies can be distinguished from drug-induced parkinsonism by its persistence after the medication has been discontinued. The extrapyramidal features in dementia with Lewy bodies are typically include rigidity, bradykinesia, a mask-like facies, stooped posture and a slow, shuffling gait. A resting tremor, as this patient had, may occur, but is unusual. Abnormalities of extraocular movement have also been reported.[5]

The visual hallucinations in cases of dementia with Lewy bodies are typically recurrent and detailed and involve people or animals. Visual hallucinations are the psychiatric manifestation that most reliably distinguishes it from vascular dementia or Alzheimer's disease, but nonvisual hallucinations may also occur. These hallucinations usually appear during periods of confusion or diminished consciousness. Additional features that support the diagnosis include repeated falls, syncope, transient loss of consciousness and delusions. Patients are often drowsy, with decreased awareness of their surroundings and episodes of total unawareness. The excessive daytime drowsiness is often accompanied by confusion on awakening. The memory impairment may be minor initially, but it increases with progression of the disease.

The diagnosis of Lewy body dementia has important management implications. Antipsychotic medications such as haloperidol or thioridazine should be avoided in these patients, as they can cause severe adverse reactions. This is important as these patients may be treated with these drugs because of their prominent hallucinations.[7] Newer antipsychotics such as clozapine and olanzapine that lack the dopaminergic blocking properties of traditional agents may hold promise for treating the agitation that occurs in dementia with parkinsonism.[1] In addition, the impaired postural stability and tendency to fall should prompt extra supervision. The response to L-dopa is usually disappointing.[7]

The patient under discussion exhibited many of the core features of diffuse Lewy body disease, including episodic disorientation on awakening at night. His cognitive impairment included visuospatial deficits and memory impairment. He had both visual and auditory hallucinations in which he believed there were other people in the room. He had extrapyramidal features which occurred spontaneously, and his decline in hospital may have been related to the administration of haloperidol. He had at least one fall. This is a clinical picture that is clearly consistent with the diagnosis of diffuse Lewy body disease.

Clinical Diagnosis

Diffuse Lewy Body disease

Pathological Discussion

At autopsy, the brain weighed 1590 grams. On gross examination after fixation it appeared normal. Coronal sections of the cerebral hemispheres revealed enlargement of the lateral ventricles, small hippocampi bilaterally and enlarged subcortical white matter perivascular spaces. There were nodules of grey matter of about 0.6 cm occupying the periventricular white matter bilaterally, more extensive on the left side. On sections, the substantia nigra also appeared somewhat pale.

Microscopic examination revealed senile plaques and neurofibrillary tangles in the frontal, temporal and parietal lobes (Figure 1). Lewy bodies were seen diffusely in the cortex, predominantly in the hippocampus and entorhinal cortex (Figures 2 and 3). They were particularly easily seen in the cingulate gyrus and medial frontal lobe areas. The hippocampus also showed neurofibrillary tangles and senile plaques with occasional Hirano bodies and granulovacuolar degeneration. Scattered dystrophic neurons were also seen in the CA2 area of the hippocampus. The amygdala showed scattered Lewy bodies.

Examination of sections from the basal ganglia and deeper nuclei showed occasional Lewy bodies in the nucleus basalis. Sections of the brainstem showed Lewy bodies in the substantia nigra and in the locus ceruleus (Figure 4).

Lewy bodies are round, eosinophilic intracytoplasmic neuronal inclusions. They are chiefly composed of altered neurofilaments, ubiquitin and a-synuclein. The exact reason for their formation is unclear. Lewy bodies have classically been associated with Parkinson's disease where they are found in selected brainstem nuclei, diencephalic nuclei and basal ganglia. In Parkinson's disease, their presence is largely confined to subcortical structures such as the substantia nigra and locus ceruleus.

In this case, the Lewy bodies are more widespread; they are found in the cortex, hippocampus, amygdala and nucleus basalis. This is consistent with diffuse Lewy body disease (DLBD), in which there is widespread cortical and subcortical Lewy body formation, especially in the entorhinal and anterior cingulate cortices and the brainstem. Other features of DLBD include a loss of neuronal density in the pars compacta of the substantia nigra and nucleus ceruleus, with normal neuronal density in the neocortex. Neuritic degeneration in the CA 2-3 region of the hippocampus is also characteristic of DLBD and not found in Alzheimer's disease.[6]

Lewy body pathology may occur in isolation or mixed with pathological changes seen in Alzheimer's disease. In this case, pathological features of Alzheimer's disease are seen in the cor-

tex, including senile plaques and neurofibrillary tangles, the hallmarks of Alzheimer's disease. There are also senile plaques, neurofibrillary tangles, granulovacuolar degeneration and Hirano bodies in the hippocampus. Some of these features, especially granulovacuolar degeneration and Hirano bodies may also be present in normal aged brains. Whether mixed cases such as this represent two coexisting pathological states, or a variant of Alzheimer's disease is controversial.

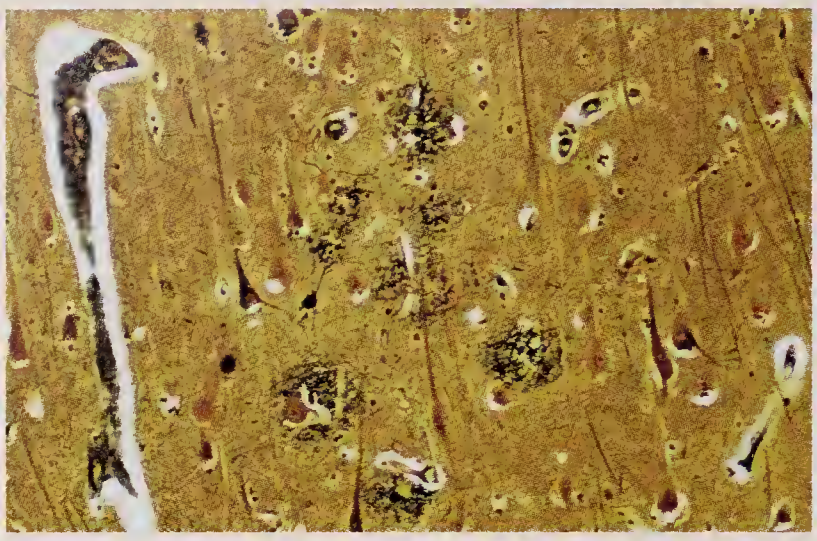


Figure 1. *Senile plaques in the neocortex (Bielchowsky silver stain x20)*

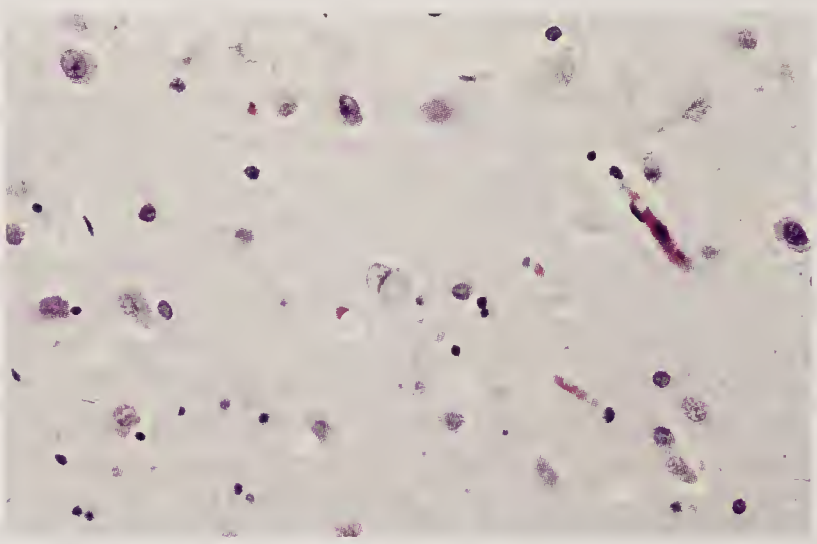


Figure 2. *Lewy bodies in the entorhinal cortex (hematoxylin and eosin x40)*

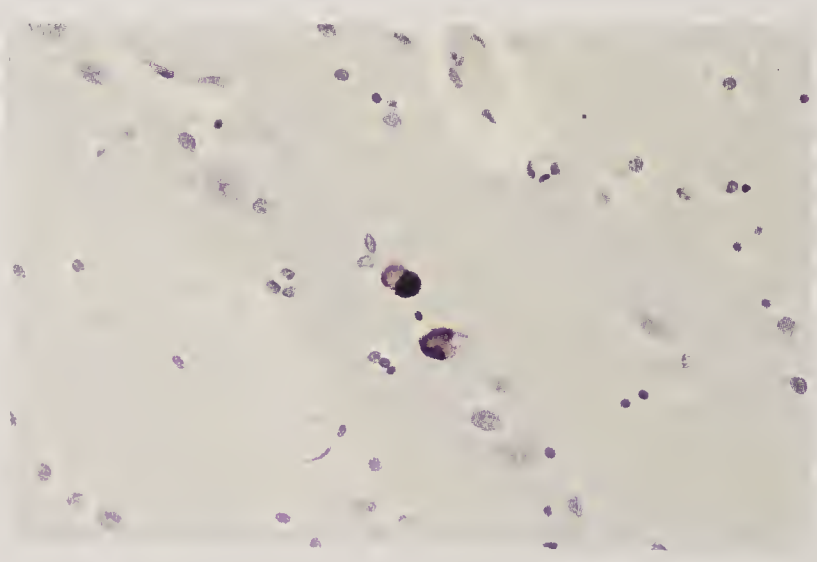


Figure 3. *Lewy bodies in the entorhinal cortex (ubiquitin antibody stain x40)*

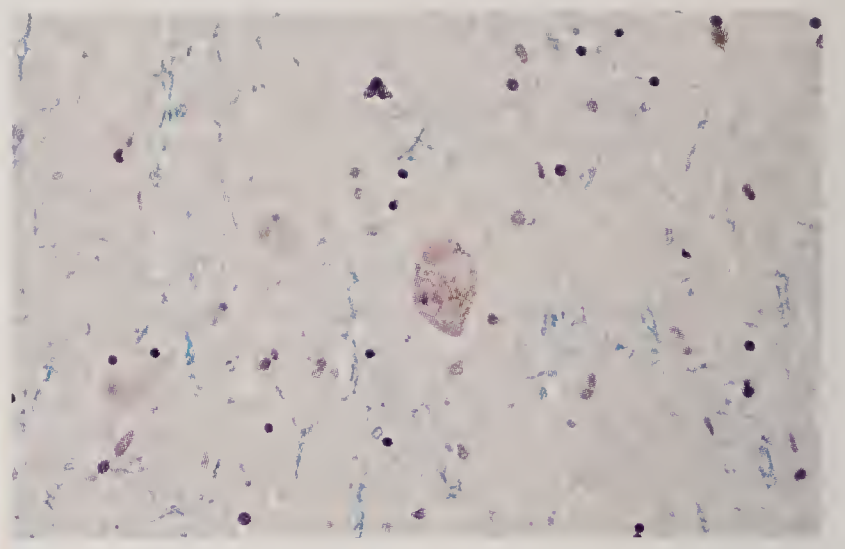


Figure 4. *Lewy body in the substantia nigra pars compacta (hematoxylin and eosin x40)*

Brain stem Lewy bodies are intensely eosinophilic and often surrounded by a pale halo. Cortical Lewy bodies, in contrast, are less eosinophilic and lack a clear halo, making them more difficult to recognize with traditional hematoxylin-eosin staining6 (compare Figures 2 and 4). Because of this, it is likely that many cases of DLBD were missed in the past. However, Lewy bodies can be stained immunocytochemically with antibodies directed against ubiquitin; this technique is twice as sensitive at detecting cortical Lewy bodies than hematoxylin-eosin staining6 (compare Figures 2 and 3). Because of this and other newer, more sensitive staining techniques, it has only recently been recognized that this disorder is common, perhaps the second most common cause of dementia following Alzheimer's disease.

The distribution of Lewy bodies in dementia with Lewy bodies can be correlated with many of its clinical features. Psychiatric symptoms may reflect the prominent involvement of the amygdala and the limbic cerebral cortex, including the cingulate, entorhinal and temporal cortex, while extrapyramidal features reflect the involvement of the substantia nigra.

Pathological Diagnosis

Diffuse Lewy body disease

Acknowledgements

The author is indebted to Drs. S. Shumak, General Internal Medicine, Sunnybrook and Women's College Health Science Centre, M. Shandling, Neurology, Mount Sinai Hospital and L. Ang, Neuropathology, Sunnybrook and Women's College Health Science Centre for their contribution to this case.

Refereneces

1. Knopman, DS (1998). The Initial Recognition and Diagnosis of Dementia *Am. J. Med.* 104(4A):2S-12S.
2. Small, GW (1998). Differential Diagnosis and early Detection of Dementia *Am. J. Geriatr. Psychiatry* 6:S26-S33.
3. Folstein, MF (1997). *Differential Diagnosis of Dementia Psychiatric Clinics of North America* 20(1) 45-57.
4. Bird, TD (1998). *Memory Loss and Dementia In: Harrison's Principles of Internal Medicine*, 14th ed., Isselbacher ED *et al.* (ed). McGraw-Hill, New York, pp.125-133.
5. McKeith, IG *et al.* (1996). Consensus guidelines for the clinical and pathological diagnosis of dementia with Lewy bodies (DLB) *Neurology* 47:1113-1124.
6. Kalra, S *et al.* (1996). Lewy Body Disease and Dementia *Arch. Intern. Med.* 156:487-493.
7. Kaye, J. A. Diagnostic Challenges in Dementia (1998). *Neurology* 51 (Suppl 1):S45-S52.

Emergency Medicine Rounds

Thomas Roger Harris, BSc., and Laura Catherine McAdam, MSc.

Case 1

A.R. Rachlis, MD, FRCP(C)
Division of General Medicine and Infectious Diseases, Sunnybrook and Women's College Health Sciences Centre

A 32 year old man who had previously been well presented to the Emergency Department with a two-day history of fever, chills, and arthralgia, then developed a petechial rash. On examination he was febrile and flushed, with left conjunctival petechiae, generalized petechiae, and a vasculitic rash. Additionally, there was evidence of tenosynovitis of his left hand and effusions of both knees (left greater than right).

FIGURE 1. *Photograph of the patient's foot.*

What is the diagnosis?

How would you manage this patient?

Case 2

J. Sarrazin, MD., FRCP(C)
Division of Radiology, Sunnybrook and Women's College Health Sciences Centre

A 42 year old man presented to the Emergency Department with an acute onset of dyspnea.

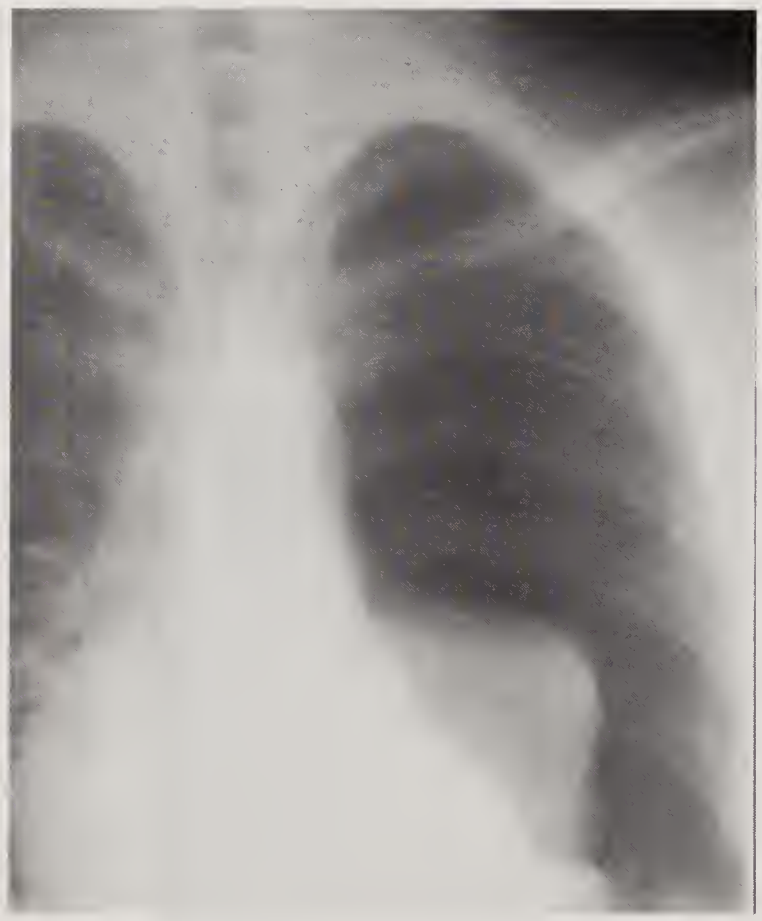


FIGURE 1. *Chest X-ray.*

What is the diagnosis?

Case 3

J. Sarrazin, MD, FRCP(C)
Division of Radiology, Sunnybrook and Women's College Health Sciences Centre

A young man presented to the Emergency Department with an acute onset of dyspnea.

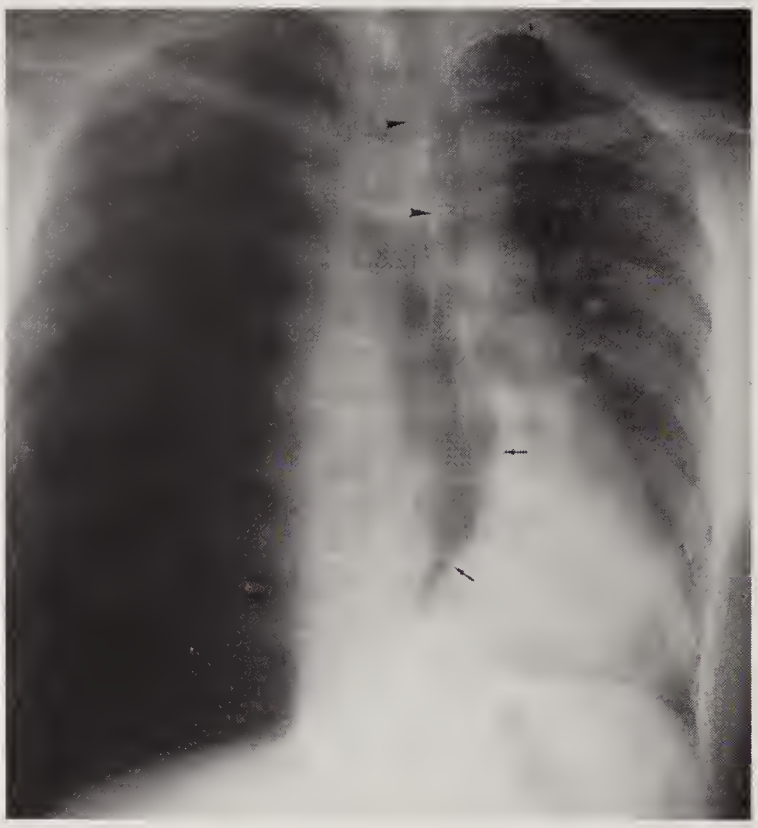


FIGURE 1. *Chest X-ray.*

What is the diagnosis?

Case 4

R. Kodama, MD, FRCSC
Division of Urology, Sunnybrook and Women's College Health Sciences Centre

A 45 year old male is involved in a motor vehicle accident and has gross hematuria. The radiograph in Figure 1 is a cystogram done through his foley catheter.

FIGURE 1. *Cystogram.*

What is the diagnosis?

Case 5

Dr. Alan Lossing, BSc., MD, FRCSC
Vascular Surgery, St. Michael's Hospital

A 29-year-old female involved in a MVA presents with a wide mediastinum on chest x-ray (Figure 1). She has neurological deficit, the blood pressure is 120/70 in both arms and the haemoglobin is 12 g/L.

FIGURE 1. *Chest X-ray.*

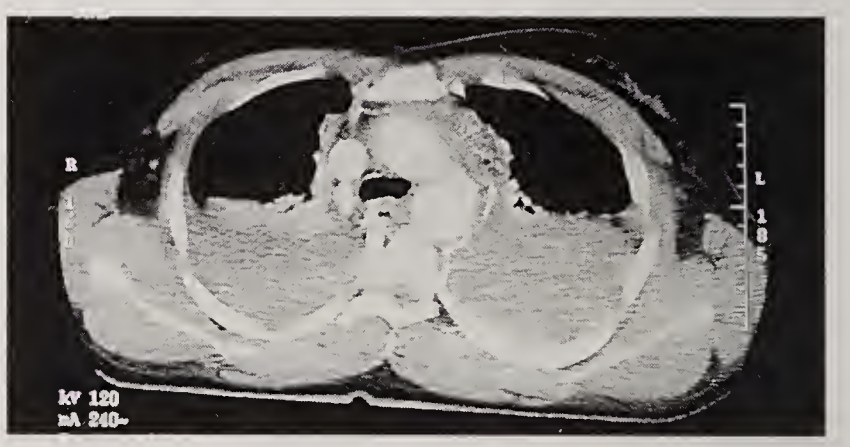


FIGURE 2. *CT scan of chest.*

FIGURE 3. *Angiogram of Aorta.*

What is the diagnosis?

Case 6

Dr. Alan Lossing, BSc., MD, FRCSC
Vascular Surgery, St. Michael's Hospital

A 70-year-old male presents with back pain and fainted at home. In the Emergency Department his blood pressure was 90 systolic with a tender abdomen. The blood pressure improved with 500cc of normal saline. The haemoglobin is 90 g/L. He was sent for a CT scan (Figure 1).

FIGURE 1. *CT scan of abdomen.*

What is the diagnosis?

FIGURE 2. *Bruise over right knee.*

FIGURE 3. *Bruise on left forearm.*

Case 7

Dr. L. Komar MD, FRCP(C), SAAP
Assistant Professor Paediatrics, Division of Emergency Medicine, Hospital for Sick Children

An 11-month-old boy presented to the Emergency Department with a 2-day history of bruising in the perineal area. According to Mom, he was learning to walk and had taken a bit of a tumble and had landed on his bottom. On examination several other bruises in various stages of healing were evident both over areas of prominence and over the chest.

FIGURE 1. *Healing bruise on right buttock.*

A What is the differential diagnosis?

B How would you manage this child?

Case 8

Dr L. Komar, MD, FRCP(C), SAAP
Assistant Professor of Paediatrics, Division of Emergency Medicine, Hospital for Sick Children

A 6-month-old black boy was brought to the Emergency Department by his father (a recent immigrant from Africa) because of crying and occasional cough. There was no history of fever, coryza and no infectious contacts. On examination, the child as somewhat cyanotic and markedly tachypneic. Examination of the chest was remarkable only for tachypnea. Cardiac evaluation was normal and the remainder of the exam was non-contributory. His O2 sat was 86% and his CXR is shown below (Figure 1).

FIGURE 1. *Chest X-ray, PA*

FIGURE 2. *Chest X-ray, LAT*

A What is the differential diagnosis?

B What in particular would you be worried about in a black child?

C How would you manage this child?

Diagnosis

Case 1

Meningococcemia

The patient was given I.V. Penicillin G, 4,000,000 units q.4.h. His family was also started on a course of prophylactic Rifampin. Over the next 10 days, the patient's fever, chills, and arthralgias resolved. Because of multiple joint effusions, the patient was seen by Rheumatology and synovial fluid was drawn off and sent for culture. He was given Indomethacin to help relieve the arthritis that had developed as a result of the meningococcemia. He showed marked improvement in all his joints, with just minimal swelling left in both knees. The patient was discharged home on a two-day prophylactic course of Rifampin and Indomethacin, 25 milligrams, to be tapered off over the course of the next two weeks.

Case 2

Massive left pneumothorax

A complete collapse of the left lung accounts for the opacity seen in the left lower thorax. An air fluid level indicates the presence of a pleural effusion.

Case 3

Right tension pneumothorax

There is a left mediastinal shift with herniation of the right lung to the left. A small air fluid level indicates the presence of a pleural effusion.

Case 4

Intraperitoneal bladder injury

This is readily seen by the dye outlining the small bowel and collecting in the right para colic gutter. The treatment of choice is primary surgical repair of this injury.

Case 5

Traumatic aortic tear

The patient involved in a motor vehicle accident with a wide mediastinum as seen on the chest x-ray (Figure 1), primary diagnosis should be aortic tear distal to the left subclavian artery. There are several methods for diagnosis including CT scan with contrast (Figure 2), transesophageal echo and angiography (Figure 3). The angiogram demonstrates an aortic tear with a false aneurysm around the tear site. Transesophageal echo allows a further delineation of the extent of the tear and if the patient has a complete aortic disruption with false lumen and in a patient with no major neurological or respiratory injury, the patient requires urgent surgical repair with an interposition tube graft. In a patient with a partial tear and significant neurological/respiratory injury, these patients should be monitored in the ICU with antihypertensive medicine.

Case 6

Ruptured Abdominal Aortic Aneurysm

The CT scan demonstrates a large retroperitoneal hematoma. This patient presented with back pain and hypotension. With a ruptured abdominal aneurysm, most often one cannot feel a pulsatile mass because of the retroperitoneal hematoma which obscures the pulsatile epigastric mass, a CT scan is contraindicated and the patient requires urgent laparotomy, aortic cross-clamping and repair of the aortic aneurysm. The mortality rate is 50 – 70% depending upon concomitant risk factors such as significant cardiac disease.

Case 7

A This case requires one to "think dirty". The bruises over the ribs on the chest are very suspicious for child abuse. However, included in the differential are bleeding disorders, such as Hemophilia.

B Blood work looking for evidence of a bleeding diatheses – a CBC + PLT count and a PT/PTT with an INR should be drawn. While the blood work is being processed, this child should undergo a skeletal survey for evidence of any occult fractures (rib fractures in particular in this case were there, were bruises over ribs). If possible, an expedient referral should be made to a Suspected Child Abuse & Neglect service. In this case, this child was diagnosed with Hemophilia A. However, should the blood work have been normal, this child should have been referred to the Children's Aid Society.

Case 8

A The differential diagnosis of tachypnea and cough is wide. It includes various types of Pneumonia (with viral pneumonia being the most common in childhood), Bronchiolitis and Congenital Heart Disease (Congestive Heart Failure.

- The CXR shows hyperinflation with peribronchial thickening, interstitial markings and the suggestion of a ground-glass pattern. In this case, a provisional diagnosis of Bronchiolitis was made as the child was seen in the winter in the middle of RSV (Respiratory Syncytial Virus) season.

B Sickle Cell Disease with a chest crisis.

C O2 by mask to improve O2 saturation to 95% must be administered immediately. Ventolin by mask has been shown to improve symptoms of Bronchiolitis in approximately 50% of patients. Thus a trial of Ventolin therapy should be initiated. A CBC & Diff, Sickle Cell screen and venous gas should be drawn and an IV placed for hydration. A nasopharyngeal swab for Resp Viruses should be sent.

In this case, the child was admitted and as the hypoxia was quite resistant and there was little, it any, improvement with treatment, the diagnosis of Pneumocystis Carinii in an HIV positive patient was entertained. The child was started on Septra, the diagnosis was confirmed and the child improved with treatment. Pneumocystis Carinii pneumonia is the most common serious opportunistic infection in the HIV-infected child.

Robots Designed to Aid in Surgical Procedures

Martin Jugenburg, BSc. (0T1)

Computers and technology permeate through all corners of life, in many instance they have become an indispensable part of our lives. They have also been incorporated into medicine in the form of many useful tools and gadgets. Surgical specialties are no exception. However, the future of computerized and robot-assisted surgery is still not fully realized.

Until recently, surgeries have traditionally been performed "open", requiring large incisions to access the operative site. Although it is a proven and effective approach, it is often accompanied with significant pain and trauma as well as significant costs related to treatment and lengthy hospital stays. In contrast, the recent rise of laparoscopic procedures highlights the fact that the benefits of minimally invasive surgeries cannot be ignored. Laparoscopic surgical procedures are less traumatic to patients, resulting in decreased post-operative morbidity rates, reduced length of hospital stay, and quicker recovery times. On the downside, laparoscopic surgery is labor intensive and potentially cumbersome and may be complex and difficult for surgeons to master. Therefore the next major improvement that is required of today's surgical technology is what is known in the world of computers as user-friendly technology.

The modernization of the OR has resulted in numerous medical devices that aid a surgeon, but also increase the complexity of the OR. In many instances, these devices are manually controlled and monitored by someone other than a surgeon. Computer Motion has approached this problem by developing the HERMES OR Control Center where HERMES-ready devices are computer controlled and respond to voice commands. Currently, the company manufactures two such devices: AESOP and ZEUS systems.

AESOP 3000 is the world's first FDAcleared surgical robot capable of assisting in new advanced minimally invasive cardiothoracic procedures. Surgeons use simple voice commands to control AESOP's scope movements and a steady operative view throughout the delicate procedure. It is a surgical robot capable of positioning an endoscope in response to surgeon's verbal commands.

The company is also developing the ZEUS Robotic Surgical System for new minimally invasive procedures, with the aim

to improve a surgeon's ability to perform complex surgical procedures. It consists of three surgeon-controlled robotic arms, one of which handles the endoscope and two of which manipulate surgical instruments at the operative site. Robotic instrument arms are controlled from a console using handles resembling conventional surgical instruments, while the surgeon views the operative site through a high resolution monitor. The computer interface scales surgeon's hand movements (if necessary) and filters out hand tremor. This results in precise micro movements at the operative site. The endoscope arm is voice controlled by the surgeon, thus giving the surgeon complete control over all three robotic arms of ZEUS.

Some of the achievements of the ZEUS system to date include fully endoscopic tubal reanastomosis, with all patients back to full activity earlier than with traditional open surgery. ZEUS Robotic Surgical System enables multivessel endoscopic coronary anastomoses through incisions smaller than the diameter of a pencil, while previously CABG procedures with robotic assistance have been limited to single vessel procedures. In the fall of 1998, ZEUS successfully performed it first clinical coronary artery bypass graft through pencil-sized entry sites. Later that fall, ZEUS successfully completed world's first clinical beating heart coronary bypass at the University of Grosshadern in Munich, Germany.

On the negative side, despite tactile feedback of the handles, the surgeons don't get the same 'feel' as they get using their hands, and it will likely require additional training for surgeon's to adapt to.

While ZEUS is not perfect, it is definitely a move in the right direction. Computer Motion company's products show us that the marriage of a surgeon's intelligence with a robot's precision and dexterity can lead to new and improved surgical procedures. Many anticipate a future in which robots will play an increasingly large role in medical practice; for surgical specialties, the future has arrived.

Computer Motion, Inc.
130-B Cremona Drive
Goleta, CA
USA 93117
Telephone: (805) 685-3729
Facsimile: (805) 685-9277
www.computermotion.com

MEDICAL ALUMNI ASSOCIATION
UNIVERSITY OF TORONTO

◇ The memership includes all the graduates of the undergraduate medical program – approximately 12,000. The *Medical Alumni Association* provides a link between the graduates, their medical school and their university.

◇ The Mandate of the *Association* is to preserve and enhance the educational experience of the medical student body of the Faculty of Medicine through:
- student loan program
- scholarships, bursaries, awards and prizes
- travel grants
- other student projects

◇ The Medical Class reunions are assisted by our secretarial services.

◇ The *Medical Alumni Association* liases with the Faculty of Medicine and the University of Toronto.

Medical Alumni Association
Room 3249
Medical Sciences Building
Toronto, Ontario M5S 1A8
(416) 979-1539

Executive Director
Dr. Tom Patterson

Administrator
Susan Underhill

the pharmacy & drug Basics

We are a Growing Pharmacy Chain, Providing Lower Costs to You and Your Patients, with "Service You Can Trust."

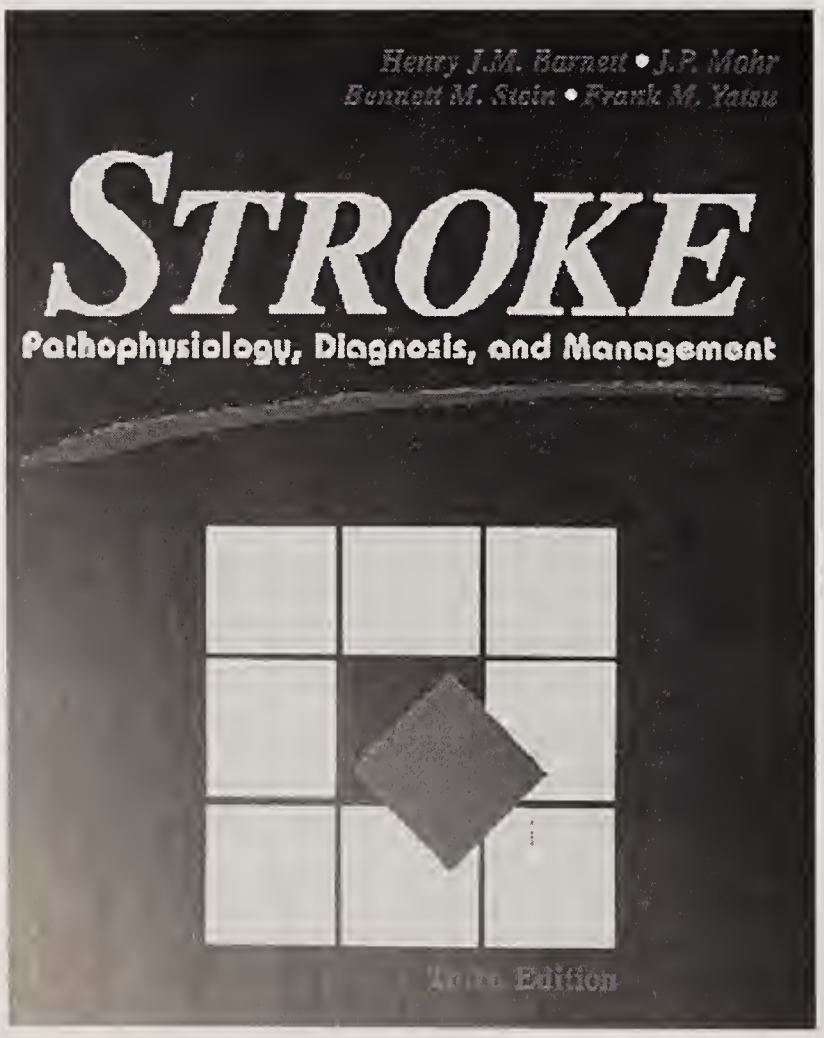
A&P Drug Mart Ltd.
5559 Dundas Street, West
Islington, Ontario
M9B 1B9
416-234-6943
Fax 416-234-6581

Stroke: Pathophysiology, Diagnosis, Management, Third Edition

Reviewed by David M. Kaplan (OT1)

Editors: Barnett H.J.M., Mohr J.P., Stein B.M., Yatsu F.M.,
Publisher: Churchill Livingston
Date of Publication:1998
Number of Pages:1459 pages

Overall Rating:	8.5/10
Strengths:	Aside from the wealth of useful information in this book, the excellent organisation makes finding the right information easy. The book also includes numerous, high-quality reproductions of radiological studies.
Weaknesses:	While the book covers stroke in the young adult (15-49), it does not include a separate section on stroke in the paediatric population. Some of the reproduced graphs are not of the quality expected.
Audience:	medical students, residents, staff physicians, and academics



In the third edition of *Stroke*, Barnett *et al.* have revised their text to include the latest knowledge and developments in this field of neurology and neurosurgery. The text covers stroke pathophysiology, diagnosis, and therapy. The editors sought out and obtained the participation of experts in the field from all over the world; the international enthusiasm of the work is, as the authors note, "satisfying."

This new edition of *Stroke* retains its old organization; the text is logically divided into sections on pathophysiology, diagnosis, clinical manifestations, medical therapy, and surgical therapy. There is even an introductory chapter on the epidemiology of stroke. Unlike most texts, the colour plates are included at the beginning of the book.

Not only does the pathophysiology section of the text include well written chapters on neurochemistry, molecular biology, and pathology, but it also includes insightful chapters on PET and functional MRI studies. Moreover, there is also a detailed, yet very readable, chapter on atherosclerosis.

The next section of the text, which focuses on diagnostic studies, examines the different diagnostic tools available to

the clinician: laboratory studies, CT, MRI, angiography and ultrasound technologies. The authors of these chapters provide helpful clinical techniques instrumental to the interpretation of the results of these investigations.

The section on clinical manifestations of stroke is organized using the traditional method of classifying stroke, as either ischemic or hemorrhagic. Moreover, this section also includes separate chapters on the clinical manifestations of specific neuro-vascular lesions.

The next section of the text covers the specific medical diseases associated with stroke. Surprisingly, while the text included separate chapters on migraine, hypertensive encephalopathy, moyamoya disease, and vascular trauma, it does not include a separate chapter on stroke associated with sickle-cell disease, despite the fact that a large proportion of the sickle-cell population will unfortunately suffer from stroke due to their haematological abnormality.

Finally, the last chapters of the book cover the gamut of therapy available to the stroke patients; pharmacological, medical and surgical treatments are detailed. The section concludes with a chapter on rehabilitation of the stroke survivor.

Without eliminating technical detail, Barnett *et al.* have produced a text that covers almost the entire range of stroke knowledge. Aside from the wealth of useful information in this book, the excellent organization makes finding the right information easy. Another notable feature deserving of praise are the high-quality reproductions of radiological studies.

However, while the book covers stroke in the young adult (15-49) it does not include a separate section on stroke in the paediatric population. Furthermore, from a technical standpoint, some of the reproduced graphs are not of the quality expected. However despite these minor flaws, *Stroke* would be a valuable addition to the library of anyone who works, researches or has a keen interest in this area of clinical and academic neuroscience.

MCI

FAMILY PRACTICE MEDICAL CENTRES

200 Ontario physicians have discovered the benefits of MCI's management practice.

- Busy walk-in shifts
- Short or long term
- Full or part time positions
- Locum Coverage

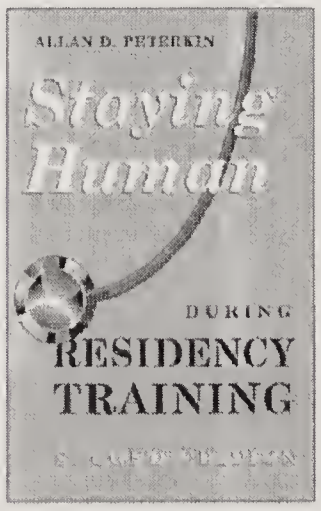
Twenty-six locations in the Greater Toronto Area
Eleven Clinics With NO Billing Restrictions

MCI MEDICAL CLINICS INC.

160 Eglinton Ave. East, Suite 200
Toronto, Ontario M4P 3B5
Heidi Rodrigues
(416) 440-4040 Ext.433
e-mail: practice@mcimed.com

Canada's Largest Medical and Health Bookstore

From *alternative medicine* to *zygomycosis*
65,000-title database at **www.lb.com/utoronto**



Medical Text and Reference Books
Course Texts, Board Reviews
Handbooks and Manuals
Large selection of general interest books in medicine, nursing, dentistry, rehabilitation, surgery, pharmacy and more. Diagnostic instruments, lab coats and examination gloves and a
Special Order Service!

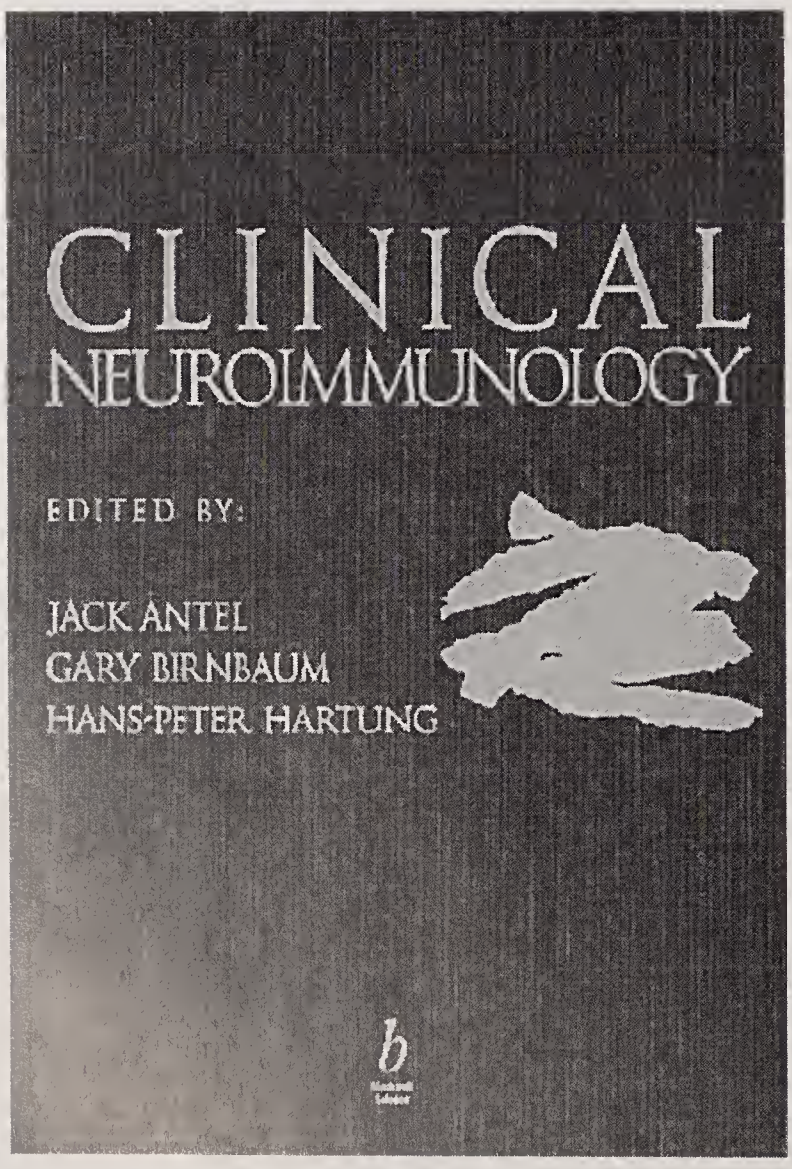
University of Toronto Bookstore
214 College St. Toronto M5T 3A1
Mon-Fri 8:45-6 Sat 10-5 Sun 12-5
Tel: (416) 978-7911 1-800-387-4420
Fax: 978-7242 1-800-665-8810

Clinical Neuroimmunology

Reviewed by Paul S. Giacomini (0T1)

Editors: Jack P. Antel, Gary Birnbaum, Hans-Peter Hartung
Publisher: Blackwell Science
Date of Publication: 1998
Number of Pages: 423

Overall Rating:	9.5/10
Strengths:	Extremely well written by prominent members of the neuroimmunology research community, good use of diagrams to illustrate complex concepts and mechanisms, very thorough in content
Weaknesses:	Lack of continuity between chapters, histology pictures could benefit from the addition of colour, very expensive
Audience:	Residents and Post Graduate Fellows in neurology, neurologists and neurosurgeons



Clinical Neuroimmunology is an excellent text for the neurology enthusiast, however somewhat misleading in its title. Although this textbook is a superb source for relevant, up to date information regarding all facets of neuroimmunology, it is not the clinical manual that its title implies. This book is targeted at physicians, but only those with an interest in complex neuroimmunological mechanisms, neuroscience research or the sub-specialist who requires an authoritative text on the subject.

Clinical Neuroimmunology is extremely well written such that even an undergraduate medical student with a limited background can appreciate it. However, the book is not geared toward this population, as the text delves into the complex interplay of immune cells in the central nervous system to a degree far beyond the scope required for the undergraduate medical student. However, this book may be a wise addition to the library of a budding neurologist with an interest in research.

The text is divided into twenty six chapters each focusing on a specific aspect of neuroimmunology. The chapters are written in the style of a textbook, yet the copious references lend them a texture similar to that of a review article. Each chapter is written by a prominent researcher in the field, frequently someone who was integral in the discovery of the concepts being described. This initially made me skeptical, as

I feared that the quality of the writing would suffer through excessive jargon or detail. However, much to my surprise and pleasure, most chapters were clear and concise. The content rarely progressed beyond the point of comprehension, quite a feat for such a specialized text. Moreover, each chapter is thoroughly referenced, drawing from recent, relevant articles that focus on the latest intriguing discoveries, and controversies, in the field.

The book covers a broad range of topics including autoimmunity, immunology of multiple sclerosis, inflammation and complement in Alzheimer's disease, HIV and related neurologic diseases, paraneoplastic neurological disorders and even the neurological sequelae of Lyme disease. Each chapter stands alone, hence reading a chapter does not necessitate understanding of preceding chapters. Although the initial chapters do provide a synopsis of the fundamentals and pertinent facts necessary to understand neuroimmunology, many of the later chapters lack continuity with one another. Unfortunately, this is an unavoidable problem when dealing with a text involving the many diverse topics in the realm of neuroimmunology. Despite this lack of homogeneity, the editors do an admirable job of maintaining a sense of cohesion throughout the book lending it an almost seamless flow.

The crowning glory of this textbook lies in its depth and breadth of content. Although neuroimmunology seems particularly focused, the plethora of topics in this field makes the synthesis of a single compendium quite a trying chore. The editors manage to circumvent this problem through clever organization, creating a textbook which covers a considerable scope without sacrificing detailed explanations or extensive coverage of each topic. This achievement, coupled with the aforementioned strengths, makes *Clinical Immunology* a truly remarkable textbook and one worth owning.

Overall, this is a fantastic book which is exquisitely well written, organized, and well -although sparsely- illustrated. Mostly simple and in black and white, the illustrations achieve their goal of highlighting pertinent features of the text and enhancing the reader's experience. The one flaw I noted regarding the illustrations was that many histology slides were black and white when the addition of colour would have been appropriate.

The one major detriment to this otherwise great textbook is its exorbitant price of $200+ (U.S.), which makes it inaccessible to all but the richest of medical students, none of whom I know. However, if you do have $300 Canadian kicking around and have an interest in neurology or the exciting and growing field of neuroimmunological research, then I would highly recommend you invest in this text.

Sinai C.A.R.E.

Consulting Associates for Resources in Education

Innovators in Healthcare Education, Sinai C.A.R.E. offers courses that are evidence based, focussed on up to date information and technology, and are led by clinical experts currently working in the field. Courses currently available that are of interest to Physicians include.

◊ Infusion Therapy - Peripheral
◊ Infusion Therapy - Central Lines
◊ Palliative Care: Pain and Symptom Management
◊ Wound and Skin Care

To be placed on our mailing list, please complete form below. If you are interested in current courses please circle above. If there are other courses you would like to be available, please list.

_____

_____

_____

Prefer: 1/2 day courses ❑ 1 day courses ❑
2 day courses ❑ Evening seminars ❑

Name_____

Address _____

City _____ Province ____ Postal Code _____

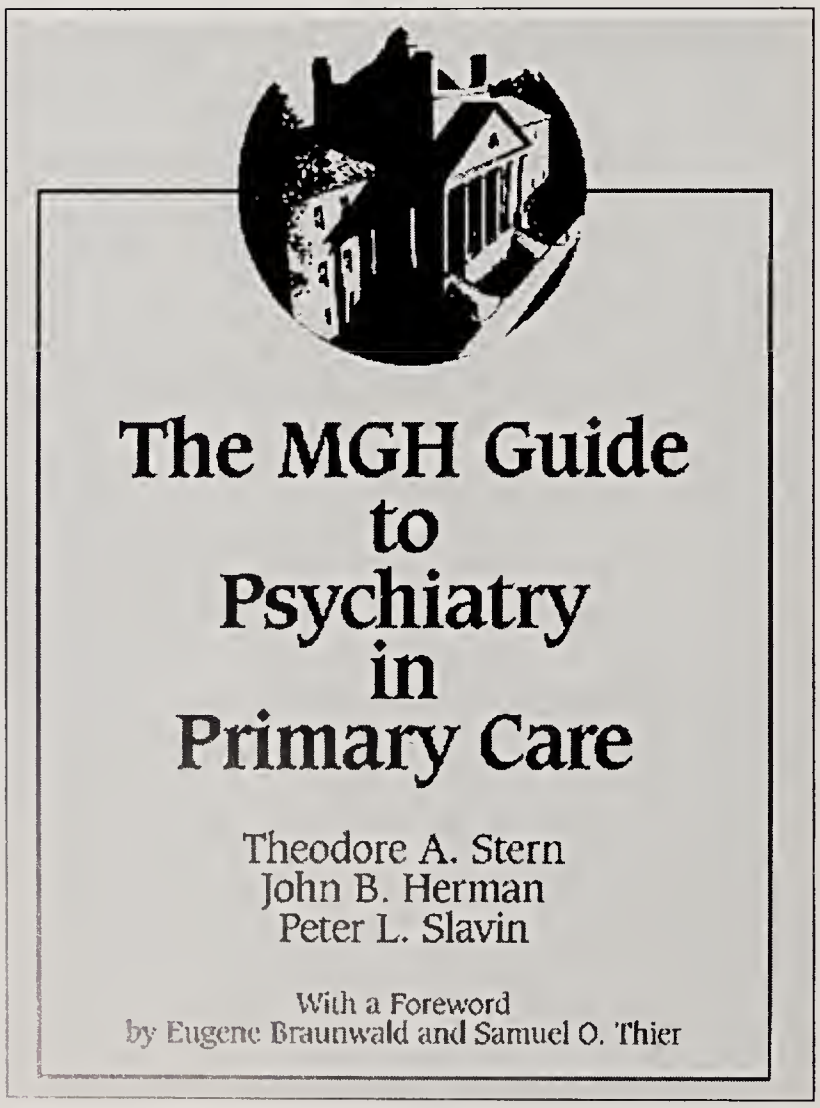
Fax completed form to 416 586 8830.

The Massachusetts General Hospital Guide to Psychiatry in Primary Care

Reviewed by Todd P. W. McMullen (0T2)

Editors: Theodore A. Stern, John B. Herman and Peter L. Slavin
Publisher: McGraw-Hill
Date of Publication: 1998
Number of Pages: 696

Overall Rating:	9/10
Strengths:	A comprehensive and practical medical resource. Well written and superbly organized.
Weaknesses:	The impressive body of information would benefit from the use of more algorithms or decision trees to summarize diagnostic and treatment strategies.
Audience:	Medical students and primary care physicians



Fully half of the visits to primary care physicians are for psychiatric problems. Many of these disorders can cause significant distress and impairment of psychosocial function. Thus, physicians are constantly challenged to identify and treat the complex constellation of physical and psychological symptoms associated with psychiatric illness. *The MGH Guide to Psychiatry in Primary Care* is an attempt to provide a comprehensive and accessible reference volume to aid in the diagnosis and treatment of such psychiatric disorders.

Intended for the primary care physician, this guide provides a practical approach to the care of the psychiatric patient. Written by a series of experts and edited by non-specialists, this book outlines the diagnosis and management of over 60 common psychiatric disorders such as anxiety, depression and substance abuse. Other notable features include discussions of homelessness, violence, smoking cessation strategies and managed care.

In general, the chapters are organized in point form outlining the scope of the illness, evaluation of the problem, differential diagnosis and treatment of the disorder. Each section is written with brevity in mind, providing a step by

step outline of how to obtain and interpret the information needed to facilitate diagnosis and subsequent treatment. Only the essentials of the condition are described, thereby preventing the chapters from becoming bogged down by prolonged digressions into pathophysiology. Important points are emphasized with boldface and tables are used appropriately to summarize risk factors, clinical features or pharmacotherapy. Thus, the wealth of information contained in this book can be accessed quickly, without having to search pages of text for clinical pearls. For those requiring additional detail or a more thorough discussion of particular disorders, each chapter also has a short reference list of current readings.

While this treatise was written for the primary care physician, it is also a useful reference for medical students and residents lacking specialized training in psychiatry. However, as a consequence of the outline format of each chapter, it is often implied that the diagnosis of psychiatric disorders is a simple extension of the listed criteria. It is important that medical students recognize that the presentation of psychiatric illness may not fit the concise criteria outlined by this book. Thus, this book is perhaps most useful to the more experienced primary care physician.

Overall, I believe that the editors of *The MGH Guide to Psychiatry in Primary Care* have created a well-written and easily accessible reference volume for the non-specialist. The primary care physician will find this guide to be a helpful resource in their daily practice.

PROFESSIONALS' PROGRAM
Dedicated to Helping You Succeed
one on ONE™
Financing to support you every step of the way
At Royal Bank, we believe in helping Canadians prosper and grow. If you are a practicing professional, or studying to become one, we can help you with the financing you need to achieve your goals.
If you're still at university
You can rely on the convenience of a Royal Bank Student Visa* Classic II Card† to help you through when you're temporarily short of cash. You may also consider a Royal CreditLine® for Students to help pay tuition and other costs while you concentrate on completing your studies.
If you're building up your practice
If you have graduated as a professional and are ready to start up, expand or improve your own practice, come in and talk to us today. We can help you with a Royal Bank Operating Line of Credit, a CreditLine for small business™, a Term Loan, Business Equipment Leasing as well as Cash Management Services.
To find out more about the Professionals' Program, please call or visit your nearest Royal Bank branch.
® Registered trade-mark of Royal Bank of Canada
™ Trade-mark of Royal Bank of Canada
* Royal Bank of Canada, licensee of trade-mark
† Subject to credit requirements
ROYAL BANK
MEMBER OF ROYAL BANK FINANCIAL GROUP

UTMJ
University of Toronto Medical Journal

INSTRUCTIONS TO AUTHORS 1999-2000

The University of Toronto Medical Journal *(UTMJ),* an official journal of the University of Toronto Faculty of Medicine, is devoted to the publication of significant, original studies and review articles in all areas of basic, clinical, translational and epidemiological medical research, as well as medical education, medical ethics, medical jurisprudence, and the history of medicine.

Procedure for Submission

Contributions should be addressed to: The Editors, *UTMJ,* Medical Sciences Building, Room 2141, 1 King's College Circle, University of Toronto, Toronto, Ontario, M5S 1A8, Canada; Phone: (416) 946-3047. The paper should be submitted by an author, preferably the principal author, who should indicate in a covering letter:

1. that the paper is being submitted for consideration for publication in the *UTMJ;*

2. the exact address to which all related correspondence should be sent and the telephone and FAX numbers at which the author can be reached;

3. that neither the submitted manuscript nor any similar paper, other than an abstract of preliminary communication, has been or will be submitted to, or published, in any other primary scientific journal;

4. that all of the authors are aware of, and agree to, the content of the manuscript and that authorization has been given to use any information conveyed by either personal communication or release of unpublished experimental data;

5. three to six key words describing the paper, to assist in the selection of the reviewers.

Original Submissions must include:

1. The author's covering letter containing the above information.

2. **Four** copies of the manuscript and **four** sets of original illustrations. Illustrations should be Camera-Ready black and white photographs, figures, line drawings, and graphs.

3. Computer diskette containing all the parts of the manuscript on **ONE** file. Refer to the following *Editing Process* section for more details.

Papers should conform strictly to *Journal* style. Any issue from Volume 75 of the *UTMJ* will provide authors with assistance in the proper arrangement of manuscripts. Papers are to be written in clear, grammatical English. Data must be presented concisely. The manuscript should be typed on 21.6-X 28- cm (8 1/2 X 11-inch) paper with double spacing throughout, allowing for 1 inch margins. Submissions should not exceed a maximum of **4000** words and shorter papers are preferred. Consecutive numbering of all pages is required, with the title page as page 1. The title page should include a) the complete names of all authors, graduate year (if from U of T), degrees, and appointments; b) the complete address to whom correspondence should be addressed; c) running title (not more than 50 characters) d) three to six key words describing the text. To facilitate the peer review process, this information must not appear on any other part of the manuscript. Make sure that the manuscript includes a contact telephone number.

Abstract

The second page of every manuscript must contain only the abstract, which should be a single paragraph not exceeding **200** words. The abstract should be comprehensive to readers, and abbreviations and reference citations should be avoided.

Sections of the Manuscript

Please subdivide original manuscripts into the following sequence of sections: Title Page, Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References, Legends to figures. Subheadings (within the Materials and Methods, Results or Discussion sections) are encouraged if they facilitate the presentation of material. Figures should be presented separately and attached to each copy of the manuscript.

References

Authors will be responsible for the accuracy of the references. In the text a reference should be cited by an Arabic superscript. The list of references should be provided in the order described above and should follow the order in which they appear in the text. References must adhere to the following style:

Journal article

1. Reinders FX, Chalin C, and Meier HMR. (1993). Alzheimer's disease: Understanding the patient and caregiver. *UTMJ.* 70(20): 16-20.

* Abbreviated journal titles should be used.

Articles **with more than 4 authors should include the first three authors followed by *et al.*

Article in a book or comparable publication

2. Norris KE, Norris F, and Brunfeldt K. (1980). *Nucleic Acids Synthesis: Applications to Molecular Biology and Genetic Engineering.* Koster H (ed). IRL Press: London, pp. 233-241.

Books, theses, or comparable publications

3. Pressaco J and Yu H. (1996). *Pharmacological Treatment of Diseases.* Urban Angel Medical Books Inc: Toronto.

Tables

Tables should be on a separate page with a short title, and be numbered and referred to in the text. Column headings and descriptive matter in table should be brief. Vertical rules should not be used.

Illustrations

Each figure should be designed to fit into an area of either one or two columns of text. Photographs and illustrations must be in black and white and of good quality. The figures, including halftones and photographs, are to be numbered consecutively in Arabic numerals, and each one must be referred to in the text as Figure 1, etc. On the manuscript indicate with an arrow in the margin the most appropriate position for the figure. Figure legends should be on a separate, numbered page and titles for figure legends should be in the form of a concluding statement. Define all symbols and abbreviations used in the figure.

Drug Names

Both non-proprietary (generic) and trade names should be provided for all drugs mentioned.

Editing Process

For the editing process we require computer diskettes along with the four copies of the manuscript. Please label the outside of the disk with *UTMJ,* the first author's name, a partial title of the manuscript and the name of the computer file and the program (MS Word 6.0; WP 5.0-6.0) used to access the manuscript on disk. When submitting revised manuscripts, authors are encouraged to send a disk of the paper along with the required four hard copy printouts. Figures are preferred both in hard copy format and disk format. Scanned photographs should be saved as TIF files and line drawing should be saved as EPS files on diskettes. Accepted manuscripts will be edited to conform with *UTMJ* style and for correctness of grammar, syntax and punctuation. Extensive error in grammar or syntax will make a manuscript unacceptable for publication. Adherence to gender neutral language is strongly encouraged. The first author will receive a copy of the edited manuscript or galley proof prior to publication and is responsible for obtaining co-authors' approval of the changes. The printers will correct the proof only for typographical errors as indicated on the proof returned by the authors. Authors are asked to take the greatest care with preparation of their papers. It will not be possible to make further alterations in the proof.

Note: It is imperative that the authors ensure that the disk file is the most recent version of the manuscript and that it matches the most recently submitted hard copy.

Review Process

Submitted articles will be reviewed by both a faculty member and a medical student, both of whom will have expertise in the field of the submitted paper. The results of this review process will then be reviewed by the Associate Editors, who on the basis of both the reviewers' comments and their own, will come to a decision as to recommend the manuscript for publication in the *UTMJ.* All rejected papers will then have a final evaluation by the Editors-in-Chief and if confirmation of rejection is established, the Editors will inform the authors of the decision of the review process. Rejected papers are encouraged to be re-submitted only if all of the reviewers' comments have been considered and corresponding changes made in the manuscript. The revised re-submitted articles will be considered new submissions and will be subjected to the standard review process by the *UTMJ.*

UTMJ
University of Toronto Medical Journal
Founded In 1923 Volume 76, No. 3 May 1999

The University of Toronto Medical Journal *(UTMJ)* is Canada's oldest undergraduate student-run publication. This year marks the 76th year of publication of the *UTMJ* and we invite you to come celebrate this formidable accomplishment by becoming a patron of the *UTMJ*.

The *UTMJ* is completely managed by the volunteer efforts of undergraduate medical students and Biomedical Communications students. The Journal is a vehicle for medical students, scientists, and health professional alike to publish original articles covering a wide range of topics. Reviews of basic, clinical, translational and epidemiological medical research, as well as medical education, medical ethics, medical jurisprudence, and the history of medicine continue to demonstrate the high caliber of writing in this publication.

The *UTMJ* allows health professionals and students to read interesting work written by former, current, or future professors, clinicians and peers. At the same time, students are permitted a much needed opportunity to gain experience publishing articles. It is through the support of the community that the *UTMJ* continues to fulfil its vital role in undergraduate life.

The success of *UTMJ* is made possible by generous support from patrons. Patronage of the Medical Journal will be subdivided into three categories: Friend of the *UTMJ* - $50.00; *UTMJ* Patron - $75.00; and *UTMJ* Benefactor - $100.00. Patrons receive three issues published during the 1999-2000 academic year, and all patrons will be acknowledged in each issue of the *UTMJ*.

Celebrate 76 years of excellence of the *UTMJ* and become a patron! Please fill in the attached form and send it with your cheque or money order (made payable to the *UTMJ*) to the **UTMJ, Room 2141, Medical Sciences Building, 1 King's College Circle, Toronto, Ontario, Canada, M5S 1A8.**

Thank you for your continuing support.

Prepayment by cheque or money order is required.

Mail cheques or money order to:

University of Toronto Medical Journal

Room 2141,
Medical Sciences Bldg.
Toronto, Canada,
M5S 1A8

UTMJ
University of Toronto Medical Journal

The official publication of The Medical Society, Faculty of Medicine, University of Toronto.
I wish to subscribe to the University of Toronto Medical Journal for one year (3 issues).

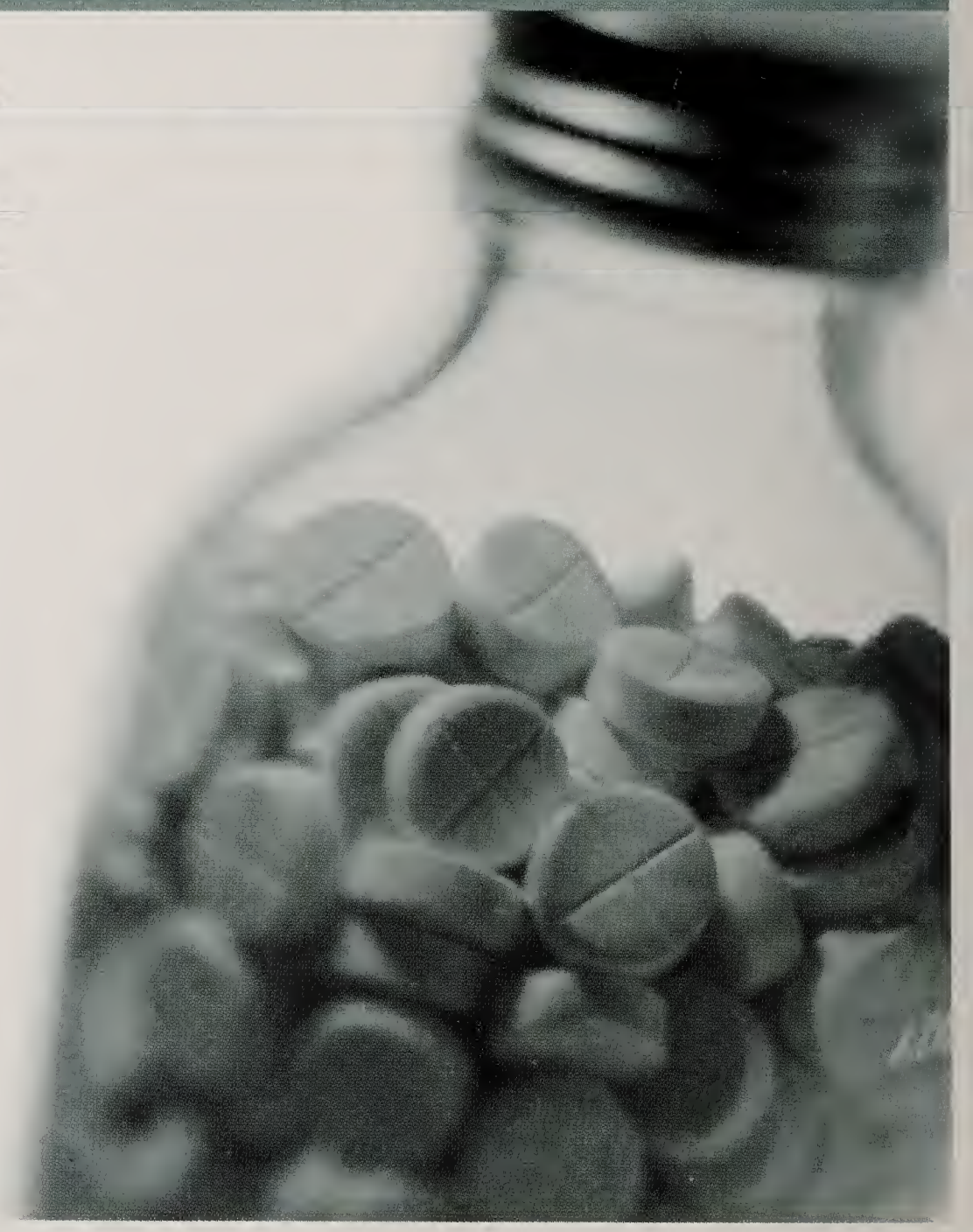
Name _____

Address _____

City _____ Province _____ Postal Code _____

If a pill saved your life, who would you thank?

Hold the door for someone and they'll thank you. Discover a medicine that saves their life and you'll never hear a word from them. That's how it is for medical researchers. The world takes them for granted. But we don't, we value them above all else. We're Canada's Research-Based Pharmaceutical Companies. Our goal is to create medicines that improve the way we live. From a simple cure for a baby's ear infection to a better treatment for heart disease. And we know the only way we'll reach our goal is through the genius of our researchers. So we thank them every day.



R&D™

Canada's Research-Based Pharmaceutical Companies

Research makes us better